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CONTENTS OF PREVIOUS NUMBER

APRIL 1945. NUMBER 4

Blood Pressures in Children Between the Ages of Five and Sixteen Years. Archibald W. Graham, M.D., Chisholm, Minn., and Edgar A. Hines Jr., M.D., and Robert P. Gage, M.S., Rochester, Minn.

Initial Aerobic Flora of Newborn Infants: Selective Tolerance of the Upper Respiratory Tract for Bacteria. John C. Torrey, Ph.D., and Martha K. Reese, M.D., New York.

Treatment of the Rat Bite Fevers with Penicillin. Warren E. Wheeler, M.D., Detroit.

Celiac Syndrome: II. Fecal Excretion in Congenital Pancreatic Deficiency at Various Ages and with Various Diets, with Discussion of the Optimal Diet. Dorothy H. Andersen, M.D., New York.

Case Reports:

Complete Heart Block in an Infant Associated with Multiple Congenital Cardiac Malformations. Lieutenant Mark T. Hoekenga, Medical Corps, Army of the United States.

Roseola Infantum (Exanthema Subitum) Complicated by Hemiplegia. Jacob Rosenblum, M.D., Brooklyn.

Progress in Pediatrics:

Ascariasis: Clinical Survey of One Hundred and Twenty-Five Cases of Infection with Ascaris Lumbricoides in Children. Lieutenant Colonel Nathan H. Einhorn, Major John F. Miller and Major Lamont Whittier, Medical Corps, Army of the United States.

Abstracts from Current Literature.

News and Comment.

Book Reviews.

Directory of Pediatric Societies.

American Journal of Diseases of Children

ME 69 MAY 1945 NUMBER 5

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PROGERIA

CLINICAL, METABOLIC AND PATHOLOGIC STUDIES ON A PATIENT

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BOSTON

s aptly stated forty years ago,[1] children suf- g from progeria present a unique and weird cal picture of "immaturity upon which has ended the blight of premature senility." This ase, which first becomes manifest at approxi- ly 1 year of age in a previously healthy in- is characterized by dwarfism, by a loss of and of subcutaneous fat and by the pre- ous development of arteriosclerosis. While llent clinical descriptions of progeria are lable in the literature,[2] but little information erning the metabolic status of patients with disease has been encountered. Because it was ved that such data might cast more light on rs responsible for stunting of growth in ren and for the changes of old age, a meta- c study was undertaken on a 6 year old boy characteristic progeria.

THE SUBJECT

he patient was a member of an essentially thy family comprised of the parents and a nger brother. He was delivered by cesarian ion (because of an android pelvis) after seven one-half months of gestation. The birth ght was 2,340 Gm. During the first year of his appearance and progress approximated e of most normal infants except that, con- y to the usual course of development, no h erupted. His weight at his first birthday 7,400 Gm.

When he was about 1 year of age, the malady ch was to become so striking became manifest as a failure to gain in weight and to grow in stature. His hair also fell out, and almost imperceptibly the facies began to change from a normal to a thin, drawn-out pattern. Physicians who examined him at 2 years (fig. 1) believed that he was suffering from ectodermal dysplasia. At about that time his first teeth appeared. Though he started to walk between the first and second year, his gait was odd, there being a tendency to sway sideways at each step. At 4 years it was noted that the fingers were always bent and could not be straightened out.

From the second to the sixth year of life he gained only 500 Gm. per year. Inquiry failed to reveal any clear explanation for this poor rate of gain, such as inadequate dietary intake, diarrhea, serious or chronic infections, renal disease or other obvious disturbances. On the contrary, his health in the usual sense of the word was excellent, as were his appetite and diet. The stools were said to be large but not otherwise remarkable. It was observed, however, that he tired easily and wished to rest for about one hour out of every three during the daytime.

At 6½ years he was admitted to the hospital for the studies reported here. The photographs of figure 2 describe better than words the fanciful and strange appearance of this dwarf. Body measurements, compared with the average normal measurements for a boy of the same age, were as follows:

	Patient	Average Normal Boy of 6 Years
Body weight	10.9 Kg.	21.0 Kg.
Standing height	94.7 cm.	118.0 cm.
Lower measurement (pubis to heel)	42.5 cm.	
Circumference of head	48.0 cm.	51.3 cm.
Circumference of chest	48.0 cm.	55.1 cm.
Circumference of abdomen	49.0 cm.	49.3 cm.

Intellectually he appeared to be unusually bright and alert.

It seemed that his superficial appearance was due largely to a remarkable lack of subcutaneous tissue. Except in the area around the groin, almost no tissue lay between the skin and the underlying muscles or bone. The skin over the

This work was supported by grants from the Commonwealth Fund of New York and the Permanent rity Fund of Boston.

From the Department of Pediatrics, Harvard Medical ool, The Children's Medical Service of the Massa- setts General Hospital and The Infants' and Chil- 's Hospitals.

1. Guilford, H.: Progeria—A Form of Senilism, ctitioner **73**:188, 1904.

2. Mitchell, E. C., and Goltman, D. W.: Progeria: ort of a Classic Case with a Review of the Literature e 1929, Am. J. Dis. Child. **59**:379 (Feb.) 1940. lford.[1]

skull and the extremities was thin, smooth and pale; over the chest and especially over the abdomen it was thick and taut and mottled with a coarse yellow discoloration. There was a total absence of hair, including eyebrows and lashes, except for a few fine hairs on the nape of the neck. A small fat pad was present under the skin over the pubis. The musculature was poorly developed. The skull was broad with prominent bosses. The fontanels were closed. The eyes appeared to be of normal size for a child of his age but were abnormally large in relation to the

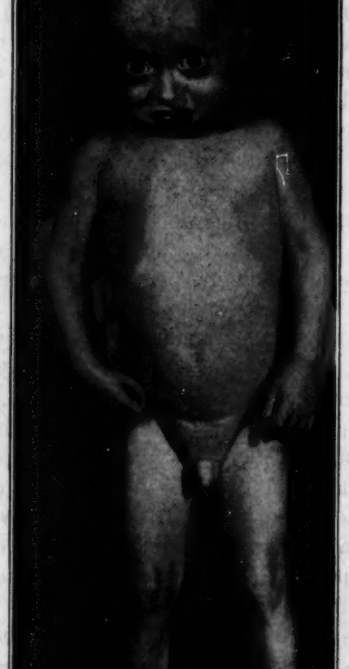


Fig. 1.—Patient at 2 years of age. The mottled appearance of the skin over the abdomen is shown. Note that there was still a small amount of subcutaneous tissue over the extremities.

rest of the face. The globes also appeared to be set far forward in shallow orbits. The joints were restricted considerably in their motions. The toes and fingers had bulbous thickenings. Two consultants, Dr. C. Larson and Dr. M. Ropes, believed these to be due to bony prominences rather than to periarticular thickening. However, so far as could be determined, the stiffness of the joints was not due to intri articular disease but more likely was a re of ligamentous thickening, as in arthrogryp

A systolic bruit could be heard all over skull and was loudest over the temporal regi A consultant, Dr. D. Cogan, thought that ex ocular movements and pupillary reflexes w normal. Vision was approximately 20/20 in e eye. The visual fields were normal. The fu could be seen easily through clear media. T left disk was normal; the right was blurred slightly elevated. The vessels were normal appearance. The upper respiratory passages ears were not remarkable. The mouth contai twenty teeth in excellent condition. The thy

Fig. 2.—Patient at 6½ years of age and before ceiving testosterone. Note the flexion deformities the joints and the prominence of the outlines of muscles and ribs due to the absence of subcutane tissue, except over the abdomen, where the skin abnormally mottled.

was easily palpable but did not appear to be abnormal consistency or size. There was thrill or bruit over the thyroid lobes. The ch was small, with flared ribs and a small clavicu spread. The lungs were clear and resonant. T heart was of normal size; the sounds were for ful; no murmurs were heard. The blood pr sure was somewhat elevated, 125 mm. of merc systolic and 85 diastolic; the pulse rate was beats per minute. The peripheral circulati

poor, as evidenced by cool extremities, which of a dull gray-pink color. Peripheral ies were firm and easily palpable. The ab- n was full and tense; no enlarged organs or rmal masses could be made out. The alia were of normal size and development he patient's age.

complete neurologic examination revealed efinite abnormalities.

amination showed the urine to be normal. hemoglobin content, the red and the white cell counts and the blood smear were not rkable. The serum sodium was 141 milli- valents per liter, the serum chloride 100 and serum potassium 4.7. The calcium was 9 and the serum inorganic phosphorus 5.8 per hundred cubic centimeters. The serum ine phosphatase was 3.9 Bodansky units. serum protein was 7.3 Gm. per hundred centimeters. Dextrose and vitamin A toler- tests gave normal results. The serum sterol level varied between 170 and 300 mg. hundred cubic centimeters. Electrocardio- s and electroencephalograms showed no ite abnormalities.

entgenograms of the entire skeleton, in- eted by Dr. R. Schatski, revealed the fol- g noteworthy features: The sutures of the were narrower than usual for a patient his the mandibles were unusually small, and was underdevelopment of the coronoid and loid processes; the bones of the extremities small; the epiphysial lines appeared defi- narrower than usual; lateral views of the showed an unusual degree of anterior ing; the shafts of the femurs were narrow, ntradistinction to wide femoral necks; the of the femoral neck was a continuation of xis of the shaft; the pubic and ischial bones completely and precociously united; the tal age estimated from the hand and wrist sponded to the normal for a 6 year old boy rding to Todd's standards, and most of the s of the body appeared to be poorly mineral- Especially notable was the lack of sub- neous tissue. A roentgenogram of the arms n when the patient was 2 years old (fig. 3*A*) ated that he possessed a visible amount of utaneous tissue at that time, while a similar tgenogram taken when the patient was 6½ s old revealed none (fig. 3 *B*).

t the chronologic age of 7½ years, his men- ge according to the Lincoln hollow square was 9 years, according to the Stanford-Binet 10½ years and according to the Healy rial completion test II 13¾ years. The iner, Dr. E. M. Hinks, believed that his ligence quotient might well advance to the "genius" level when he learned to read and write at the level of his intelligence and interests.

METHOD OF METABOLIC STUDIES

During the periods in which metabolic measurements were taken the patient lived in the metabolism ward of the Massachusetts General Hospital. He was allowed to live a normal daytime life with mild physical activity.

During the study he ingested weighed diets, the estimated contents of which are listed in table 1. Diet A was eaten during the twelve days preceding period 1, as well as during the three day periods 1 through 15 represented in figure 4. Diet B, which differed from diet A only in its fat and carbohydrate content, was ingested during periods 16 through 25. Diet C, which was constructed by the addition of more milk to diet A,

Fig. 3.—The roentgenogram of the arm (*A*) taken at 2 years reveals an appreciable layer of subcutaneous tissue; that (*B*) taken at 6½ years shows that the subcutaneous tissue previously visible has disappeared. Poor mineralization of the bones is also evident in this film. The skeletal development corresponds to the normal for the chronologic age in both films.

was taken during periods 26 to 29. Five drops of Navitol (a preparation of fish liver oils), 5 mg. of thiamine hydrochloride, 0.5 mg. of pantothenic acids (as calcium pantothenate), 1.5 mg. of riboflavin, 10 mg. of nicotinic acid, 0.5 mg. of pyridoxine hydrochloride and 1.2 mg. of paraaminobenzoic acid were ingested daily.

The stools, marked with carmine, were collected in six day lots corresponding in point of time to two three day periods. The urine was collected daily, with 5 cc. of toluene used as a preservative. Prior to analysis the urine was pooled in three day batches, two of which corresponded to one six day stool collection. Most samples of blood were obtained before breakfast, while the patient was fasting.

Most of the analytic procedures employed were the same as those used previously.[3] Other methods of determination employed were those used by Talbot and co-workers [4] for protein-bound serum iodine, by Johnston and Newburgh [5] for insensible weight loss and by Fiske and Logan [6] for calcium.

RESULTS AND COMMENTS

The studies were planned to answer certain questions.

1. Could the failure to grow and gain and the loss of subcutaneous tissue be attributed to malnutrition?

Information pertinent to this question is provided by the data of foreperiods 0 to 3, outlined

0.56 Gm. of nitrogen, which equals 7 per of the daily nitrogen intake (8.29 Gm.). ilarly, the fecal fat (7.6 Gm.) was 13 per of the daily fat intake (57.2 Gm.). Since stools of normal infants of 6,000 to 8,000 contain from 7 to 17 per cent of the nitrogen from 14 to 20 per cent of the fat ingested appears that this patient efficiently assimi these two types of nutrients. Therefore, can be assumed that the digestion and absor of carbohydrate also corresponded to the no it should be possible to make a direct compa of his caloric intake with that of other pe of similar body weight.

TABLE 1.—*Daily Diet*

Period Number * (Inclusive)	Diet	Daily Intake CHO, Gm.	Fat, Gm.	Protein, Gm.	N, Gm.	K, mEq.	Ca, Gm.	P, Gm.	Na, mEq.	Cl, mEq.
1 to 15	A	98.7	57.2	51.8	8.29	56	0.801	1.03	42.3	47.3
16 to 25	B	134.9	59.2	51.8	8.29	56	0.801	1.03	42.3	47.3
26 to 29	C	164.6	80.9	69.6	11.14	77	1.438	1.53	58.6	63.5

* Each period was of three days' duration.

TABLE 2.—*Average Daily Urinary and Fecal Excretion of Nitrogen and Certain Minerals*

Period Number * (Inclusive)	Diet	Therapy †	Daily Urinary Excretion N, Gm.	K, mEq.	Ca, Mg.	P, Mg.	Na, mEq.	Cl, mEq.
0 to 3	A	None	7.48	49.3	109.0	518	44.2	50.0
4 to 9	A	Me-T	5.76	44.3	74.2	425	42.0	50.0
10 to 15	A	T-P	6.44	42.8	43.0	459	40.6	50.1
16 to 19	B	T-P	6.00	40.5	48.0	426	40.0	49.5
20 to 25	B	T-P & E-B	6.45	42.6	53.2	523	40.1	48.9
28 to 29	C	T-P	7.53	51.0	151.0	653	40.5	55.1
			Daily Fecal Excretion					
1 to 14	A, B	.....	0.56	4.9	540	350	—	0.5
27 to 29	C	T-P	0.72	5.1	640	340	—	0.8

* Each period was of three days' duration. The period numbers of this table correspond to those of figure 4 only.
† Me-T indicates the oral administration of 50 mg. of methyl testosterone daily; T-P indicates the intramuscular administ of 25 mg. of testosterone propionate daily; E-B stands for the daily intramuscular injection of 1.66 mg. of estradiol be

in tables 1 and 2. It is seen that the patient by choice ingested approximately 1,120 calories (103 calories per kilogram of body weight) daily. It is also noted that the stools contained

A calculation of balances from the da tables 1 and 2 shows that on the average output of nitrogen, potassium, calcium, p phorus, sodium and chloride in the urine stools corresponded closely to the intake of t substances.[8] Certain of these balances are

3. Talbot, N. B.; Butler, A. M., and MacLachlan, E. A.: The Effect of Testosterone and Allied Compounds on the Mineral, Nitrogen and Carbohydrate Metabolism of a Girl with Addison's Disease, J. Clin. Investigation **22**:583, 1943.

4. Talbot, N. B.; Butler, A. M.; Saltzman, A. H., and Rodriguez, P. M.: The Colorimetric Estimation of Protein-Bound Serum Iodine, J. Biol. Chem. **153**: 479, 1944.

5. Johnston, M. W., and Newburgh, L. H.: The Determination of the Total Heat Eliminated by the Human Being, J. Clin. Investigation **8**:147, 1930.

6. Fiske, C. H., and Logan, M. A.: The Determination of Calcium by Alkalimetric Titration, J. Biol. Chem. **93**:211, 1931.

7. Levine, S. Z.; McEachern, T. H.; Whe M. A.; Marples, E., and Kelly, M. D.: Respir Metabolism in Infancy and in Childhood: XV. Energy Requirements of Normal Infants, Am. J Child. **50**:596 (Sept.) 1935.

8. It is of interest that none of the individual day average values of periods 0 to 3 differed fro mean value for these four periods by more than cent. This observation not only attests the acc of the patient's regimen, but indicates that he was remarkably stable state with respect to the intak output of the substances measured. While this st

(Footnote continued on next page)

in figure 4, which also shows that during welve days of foreperiods 0 to 3 the patient er gained nor lost weight.

cording to the Committee on Foods and ition of the National Research Council, an e of 100 calories per kilogram of body ht per day is adequate to meet the energy growth requirements of infants 1 year of At 1 year most infants weigh approxi- ly 11,000 Gm., which is the weight of this nt. A similar value for total caloric intake described by Levine and his associates, who dealing with normal infants weighing to 8,000 Gm.[7] Furthermore, the caloric e per kilogram tends to decrease as the body ht and age increase.[9] Accordingly, the in- of 103 calories per kilogram by this patient ld have been adequate for normal growth as as for energy requirements. Yet he did row. This failure to grow suggests that dur- hese periods the caloric output was equal to caloric intake.[10] The fact that he was in ral and nitrogen balance also suggests that as not gaining or losing body tissue. Thus patient used approximately 100 instead of normal 85 calories per kilogram to meet daily requirements for total energy and rmediary metabolism.[7] It was also found his basal energy metabolism amounted to calories per day, or 95 calories per kilo- n per day, as compared with approximately to 700 calories per twenty-four hours, or t 60 calories per kilogram daily for the nal 11,000 Gm. child.[11]

hese data suggest that this patient was suffer- from malnutrition not in terms of dietary ke or absorption but rather in the special e that his abnormally elevated expenditure eat and energy utilized approximately all energy derived from the diet and thus left st nothing available for growth.

Was this elevated energy metabolism due yperthyroidism?

In common with hyperthyroid children,[12] this patient had signs of hypermetabolism, such as elevated basal metabolic rate, tachycardia, mild hypertension, tendency to hyperhidrosis and failure to gain in weight. On the other hand, he did not manifest other symptoms and signs characteristic of hyperthyroidism, such as nervousness or emotional instability, enlargement of the thyroid, a thyroid bruit or thrill, tremor of the extended fingers, generalized weakness and

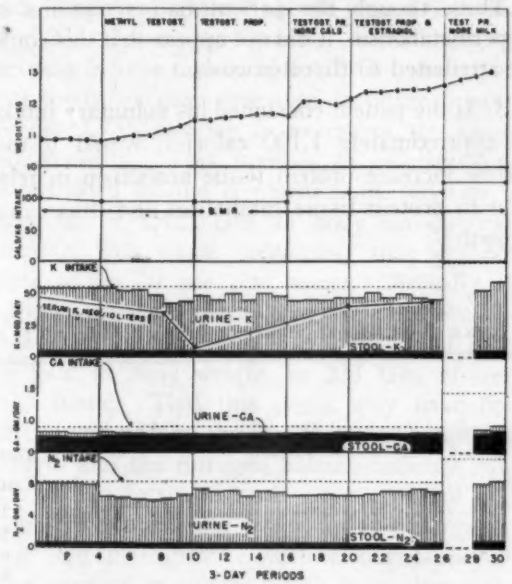


Fig. 4.—Metabolic observations before and during testosterone therapy. The regimen is indicated by the uppermost section. Changes in body weight are indicated by the solid circles connected by solid lines. In the next lower section, crosses connected by lines give the caloric intake. The underlying shaded area indicates the basal energy metabolism. The lower three sections of the figure give the daily intake (horizontal broken line), urinary output (vertical lines) and fecal output (solid black) of, respectively, potassium, calcium and nitrogen. Scales corresponding to each of the foregoing measurements are presented along the left ordinate. When the line indicating the total fecal and urinary output of a substance reached the line representing the intake of that substance, the patient was in equilibrium with respect to that substance; when the line giving the fecal plus urinary output was lower than the intake (as in periods 4 to 25), the patient was storing the substance at a rate equal to the width of the space between the upper intake line and the lower line defined by the urinary plus fecal output. Also presented in the figure are measurements of the serum potassium (solid line connecting solid circles running through the portion of the chart indicating urinary potassium) expressed as milliequivalents per 10 liters according to the scale given for potassium intake and output along the ordinate.

ot unusual for nitrogen and potassium balances, extraordinary for sodium and chloride balances mble, J. L.: Chemical Anatomy, Physiology and ology of Extracellular Fluid: A Lecture Syllabus, rtment of Pediatrics, Harvard Medical School,). Possibly this stability is a characteristic of per- with little subcutaneous tissue.

Butler, A. M.: Nutritional Requirements in In- y and in Childhood, Am. J. Dis. Child. **64**:898 v.) 1942.

Newburgh, L. H.; Wiley, F. H., and Lashuret, H.: A Method for the Determination of Heat duction Over Long Periods of Time, J. Clin. In- gation **10**:703, 1931.

(*a*) Benedict, F. G., and Talbot, F. B.: Metab- n and Growth from Birth to Puberty, Publication Carnegie Institution of Washington, 1921. (*b*) ne and others.[7]

12. Helmholz, H. F.: Exophthalmic Goiter in Childhood, J. A. M. A. **87**:157 (July 17) 1926. Dinsmore, R. S.: Hyperthyroidism in Children: A Review of Fifty-Seven Cases, ibid. **99**:636 (Aug. 20) 1932. Crile, G., Jr., and Blanton, J. L.: Exophthalmic Goiter in a Boy Two and One-Half Years of Age: Review of Literature, Am. J. Dis. Child. **53**:1039 (April) 1937.

gastrointestinal disturbances.[12] The prominence of his eyes appeared to be due to shallow orbits rather than to the edema of exophthalmos. There was no tendency to stare, and the ability to converge the eyes was intact. Furthermore, as will be shown, the concentration of protein-bound iodine in the serum was within normal limits. Finally, the administration of iodine to another progeric patient (fig. 7) was without effect on the course of his disease.

Thus, though the patient had symptoms of hypermetabolism, it did not appear that this could be attributed to thyrotoxicosis.

3. If the patient consumed his voluntary intake of approximately 1,100 calories, would testosterone increase protein tissue anabolism in relation to protein tissue catabolism and thus cause growth?

especially of nitrogen, potassium and phos- us. Finally, a definite increase in the di intake (diet C, periods 26 to 29) while patient continued to receive testosterone pionate alone resulted in strikingly more po balances of all the substances measured. was reflected in an increase in the rate of in body weight from 20.8 to 52.5 Gm. per

These observations show that testostero capable of inducing growth in a patient progeria. In fact, the gain in body weight d this seventy-two day period of testosterone apy was equal to more than one fifth o initial body weight. It would appear that a small portion of this gain in weight s be attributed to the increased caloric intak diets B and C.

In a previous paper[3] it was concluded each gram of nitrogen retained indicates

TABLE 3.—*Changes from Foreperiod Balances* (Periods 0 to 3) Induced by Various Forms of Ther*

Period Numbers	Diet	Therapy†	Gain in Body Weight per Day, Gm.	Average Daily Balance				
				N, Gm.	K, mEq.	Ca, Gm.	P, Gm.	Na‡ mEq.
4 to 9	A	Me-T	41	+1.72	+ 5.0	+0.035	+0.093	+2.2
10 to 15	A	T-P	20.8	+1.04	+ 6.5	+0.066	+0.059	+3.6
16 to 19	B	T-P	20.8	+1.48	+ 8.8	+0.063	+0.092	+4.2
20 to 25	B	T-P+ E-B	20.8	+1.03	+ 6.7	+0.058	—0.005	+4.1
28 to 29	C	T-P	52.5	+2.64	+19.1	+0.500	+0.375	(+20.0)‡

* These balances were calculated from the data of tables 1 and 2.
† See footnote to table 2.
‡ These values were computed from values for urinary output only and thus denote changes from the average urinary s output during the foreperiods 0 to 3. The value for periods 28 to 29 is placed in parentheses to emphasize that a constan negligible output of sodium in the stool has been assumed.

The data of figure 4 and table 3 show that the daily administration of 50 mg. of methyl testosterone by mouth (periods 4 to 9) and later of 25 mg. of testosterone propionate by intramuscular injection (periods 10 to 15) resulted promptly in a gain in body weight. With foreperiods 0 to 3 used as a base line, there was also evident a daily retention of relatively large quantities of nitrogen and potassium and of smaller quantities of calcium, phosphorus and sodium (table 3). These agents did not appreciably influence the chloride balance. The already positive balances induced by testosterone propionate were slightly to moderately increased by the exhibition of more calories (diet B, periods 16 to 19). On the other hand, when treatment with 1.66 mg. of estradiol benzoate in addition to testosterone propionate was instituted in an attempt to improve the calcium and phosphorous balances (periods 20 to 25), there resulted a tendency toward less strongly positive balances,

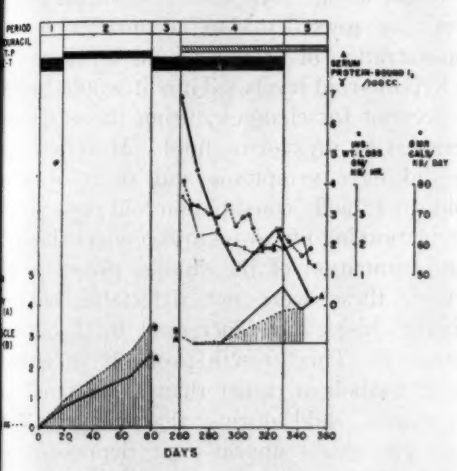
formation of 28.6 Gm. of true muscle.[13] L wise, because true muscle normally contains proximately 100 milliequivalents of potas per kilogram, each milliequivalent of potas retained is representative of 10 Gm. of muscle. With such constants for nitrogen potassium available, it is possible to esti from the data on balance how much true m the patient gained under the influence of te terone therapy. Thus, since the patient wa nitrogen equilibrium during the forepe 0 to 3, during periods 4 to 9 he gained 1.72 of nitrogen daily for eighteen days, or a t of 31 Gm., and hence 890 Gm. (31 × 28.6) true muscle.[14] The total gain of true mu

13. The term "true muscle" refers to fat-free extracellular water–free muscle fibers, collagen elastin, that is, the intracellular phase describe Hastings and Eichelberger.[18]

14. Similarly during the same periods he gain total of 90 milliequivalents of potassium and h (90 × 10) 900 Gm. of true muscle.

hus been estimated for each group of thera-
c periods.

arting with the foreperiod as a base line, umulative gains in muscle (curve B) and dy weight (curve A) are plotted in figure 5, ds 1 and 2. A scale in kilograms is given the left ordinate. The fact that curve B above curve A indicates that the patient d a greater weight of true muscle (esti-d from the nitrogen balance) than he gained tal body weight. Up to the thirty-sixth of the periods described in figure 5, while as still eating diet A, he had gained 1,425 of muscle thus estimated but had gained 1,094 Gm. of body weight. By the end of y days (end of period 2, mentioned in fig-) he had gained 3,370 Gm. of true muscle [15] only 2,340 Gm. in total body weight.



g. 5.—Observations of gain in body weight (curve nd calculated gain in true muscle (curve *B*) over period of one year, according to the scale at the ordinate. In the right portion of the figure are presented measurements of the concentration of in-bound serum iodine (triangles connected by line), insensible weight loss (crosses connected ght solid line) and basal metabolic rate (white s connected by broken line), according to scales along the right ordinate. Period 1 of this figure sponds to periods 4 to 9 of figure 4; period 2 of figure corresponds to periods 10 to 29 of figure 4. d 3 indicates the interval of one hundred and eighty when the patient was at home. Periods 4 and 5 sent a second admission to the hospital not shown gure 4. The therapy for each period is indicated he horizontal columns near the top of the figure. stands for testosterone propionate; Me-T, for yl testosterone.

During the same periods of therapy he had also d potassium in a quantity equal to that present in Kg. of average normal true muscle. Despite this ent plethora of potassium, his serum potassium ntration fell temporarily from a normal value of illiequivalents per liter to the very abnormally low of 0.7 milliequivalents per liter (period 10 out-

Unless there was a diminution in the energy metabolism,[16] such a growth of protoplasm as occurred in this patient while ingesting diet A of 1,100 calories per day following testosterone therapy could take place only at the expense of energy derived from some other body tissue equivalent to the caloric value of the protoplasm gained. Thus, assuming that dry protein has a standard fuel value of 4.1 calories per gram,[17] then true muscle, which is 30 per cent protein and 70 per cent water,[18] should have a fuel value of 1.23 calories per gram. Accordingly, an increase in true muscle of 1,425 Gm. during the first thirty-six days described in figure 5 would require 1,755 calories in excess of the energy requirements. This number of calories could be provided by the combustion of 188 Gm. of body fat or 1,425 Gm. of body carbohydrate, assuming the tissue containing such carbohydrate to be 70 per cent water. Actually the patient appears to have lost the difference between 1,425, the gain in true muscle, and 1,094, the gain in body weight, or 331 Gm. of some body tissue. That this tissue may have been fat is suggested by the fact that the data on the mineral and the nitrogen balance indicate gains rather than losses of such other types of body tissues as extracellular water, intracellular water, bone and glycogen.[19] Such a possibility also finds support in studies which have shown that when growing dogs receive too little energy-producing substance in their food the skeleton may grow and the weight increase though the

lined in figure 5). In this patient, as in others receiving testosterone,[3] there were no detectable clinical manifestations referable to the low serum potassium. (Butler, A. M.; Talbot, N. B., and MacLachlan, E. A.: Effect of Testosterone Therapy on Concentration of Potassium in Serum, Proc. Soc. Exper. Biol. & Med. **51**:378, 1942.)

16. While testosterone propionate has little or no calorigenic effect, methyl testosterone is said to increase the energy production. (Kenyon, A. T.; Sandiford, I.; Bryan, A. H.; Knowlton, K., and Koch, F. C.: The Effect of Testosterone Propionate on Nitrogen, Electrolyte, Water and Energy Metabolism in Eunuchoidism, Endocrinology **23**:135, 1938. McCullagh, E. P., and Rossmiller, H. R.: Methyl Testosterone: II. Calorigenic Activity, J. Clin. Endocrinol. **1**:503, 1941. Kinsell, L. W.; Hertz, S., and Reifenstein, E. C., Jr.: The Effect of Testosterone Compounds upon the Nitrogen Balance and Creatine Excretion in Patients with Thyrotoxicosis, J. Clin. Investigation **23**:880, 1944.)

17. Lusk, G.: The Science of Nutrition, ed. 4, Philadelphia, W. B. Saunders Company, 1928.

18. Hastings, A. B., and Eichelberger, L.: The Exchange of Salt and Water Between Muscle and Blood: I. The Effect of an Increase in Total Body Water Produced by the Intravenous Injection of Isotonic Solutions, J. Biol. Chem. **117**:73, 1937.

19. Fenn, W. O.: The Deposition of Potassium and Phosphate with Glycogen in Rat Livers, J. Biol. Chem. **128**:297, 1939.

caloric content of the animal may diminish.[20] The limited therapeutic benefit of such therapy was demonstrated by the fact that during the six months of period 3, outlined in figure 5, when the patient was living at home and was receiving 50 mg. of methyl testosterone by mouth daily, he gained only 590 Gm. in body weight, a rate of gain equal to but 1 Kg. per year.

4. Hence we turned to the question, would a therapeutic reduction in the abnormally high energy output of the patient favorably influence his ability to gain on a constant food intake?

Accordingly, at the onset of period 4 (fig. 5) he was readmitted to the metabolic ward for combined therapy with methyl testosterone (50 mg. daily) and thiouracil (50 mg. every eight hours).[21] During this period he ate a diet containing approximately 135 Gm. carbohydrate, 57 Gm. fat and 46 Gm. protein. This diet was calculated to yield approximately 1,250 calories. Changes in true muscle were estimated according to changes in the nitrogen balance, as has been outlined. In addition, changes in the energy metabolism were followed by daily measurements of the insensible weight loss[5] and by thrice weekly determinations of the basal metabolic rate. Finally, changes in the concentration of thyroid hormone in the blood stream were followed by means of determinations of the concentration of protein-bound serum iodine.[4] The values obtained for these measurements are set forth in figure 5. Scales corresponding to each measurement respectively are given along the right ordinate.

It is noted that at the onset of period 4 (fig. 5), while the protein-bound serum iodine was within normal limits (7 micrograms per hundred cubic centimeters), both the basal metabolic rate (80 calories per kilogram per day) and the insensible weight loss (3.5 Gm. per kilogram of body weight per day) were abnormally elevated.[22] It is also observed that during the first ten days of period 4 the patient was losing both body weight (curve A) and nitrogen (curve B). However, with continuance of the thiouracil therapy the basal metabolism, insensible weight loss and concentration of protein-bound serum iodine decreased somewhat; the body weight stabilized, and he was in nitrogen balance. It is of int that this stabilization occurred after a fa the protein-bound serum iodine and in the en metabolism had occurred but before the for protein-bound serum iodine had falle hypothyroid levels (less than 4 microgram hundred cubic centimeters). Later, after energy output and concentration of serum io had further decreased, he commenced to both in body weight and in body nitrogen.

This tendency to stop losing and subsequ to gain body weight and nitrogen on a stant dietary intake as the energy output di ished lends further support to the thesis an excessive total energy metabolism inter with the patient's growth. On the other h the gains recorded in period 4 (fig. 5) m be interpreted to reflect merely an accumul by myxedema.[23] It would be surprising, ever, for myxedema to accumulate before concentration of protein-bound serum iodine to hypothyroid levels. Thus it would be diff to account for changes during the early da period 4 by myxedema fluid. Moreover, th he did have symptoms and signs of hypo roidism (chiefly constipation and poor perip circulation but not gross myxedema) shortly the termination of the studies presented in ure 5, these were not detectable before Finally, his stature increased by 1 cm. du period 4. This growth probably indicates tissue anabolism rather than an accumulatio myxedema fluid during that period. Acc ingly, it would appear that depression of energy output by means of thiouracil the temporarily favored body growth.

The observations of period 5 (fig. 5) ind that growth ceased when the testosterone the was discontinued. This is not surprising view of the well known tendency for hypo roid children to be severely retarded in t growth and development.

While he was receiving thiouracil, there a gradual decrease in the pulse rate from average of 115 to 95 beats per minute. blood pressure also fell from approximately systolic and 80 diastolic to about 100 sys and 60 diastolic (millimeters of mercury). association with these changes, the veins of scalp became less prominent and the heart sou less forceful. The oral temperature did change significantly.

After about seventy days of thiouracil ther the submaxillary glands became noticeably s

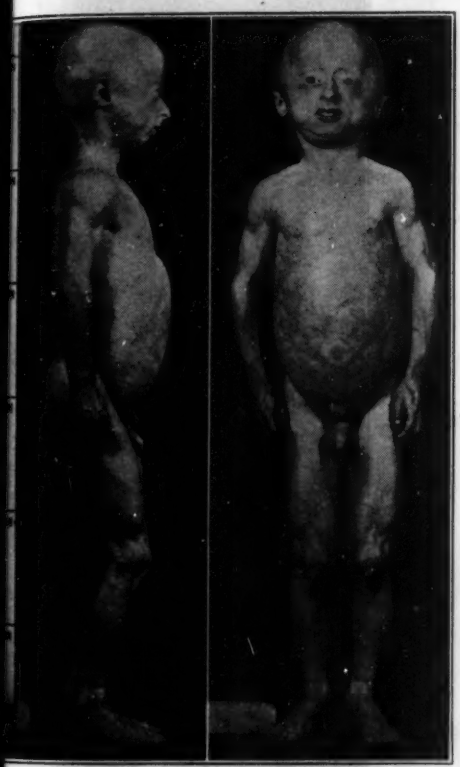
20. Aron, H.: Wachstum und Ernährung, Biochem. Ztschr. **30**:207, 1910-1911, cited by Lusk.[17]

21. Astwood, E. B.: Treatment of Hyperthyroidism with Thiourea and Thiouracil, J. A. M. A. **122**:78 (May 8) 1943.

22. Levine, S. Z.; Kelly, M., and Wilson, J. R.: The Insensible Perspiration in Infancy and in Childhood: II. Proposed Basal Standards for Infants, Am. J. Dis. Child. **39**:917 (May) 1930. Benedict and Talbot.[11a]

23. Means, J. H.: The Thyroid and Its Dise Philadelphia, J. B. Lippincott Company, 1936.

ut not red, warm or tender. Shortly after udies presented in figure 5 were completed, hyroid gland itself became noticeably en- d and of firm to hard consistency. A few later he suffered from an episode closely bling acute thyroiditis. This was charac- d by acute swelling of the thyroid and cel- s of the adjacent skin. The episode subsided ree days. During this interval, thiouracil discontinued, and 2 Gm. of sulfadiazine per was given. Thiouracil therapy was then ituted without any untoward effects.



g. 6.—Appearance of patient after approximately months of testosterone therapy. Note the obvious ase in musculature over that evident in figure 2.

FURTHER CLINICAL OBSERVATIONS

igure 6 shows the patient's appearance toward nd of the recorded studies. It is evident that ad gained considerable amounts of muscula- . This increase in musculature closely re- bles that observed when testosterone was inistered to rodents.[24] However, no in- se in subcutaneous tissue could be demon- ed either by physical examination or by opriate roentgenograms. In addition to a gain in weight of 4.75 Kg., he grew 7.3 cm. in height in the course of one year. During the course of one and one-half years of testosterone medication the skeletal development advanced rapidly to correspond to that of a 15 year old boy. Aside from these easily detectable changes, relatively few other alterations of note became evident. The previously high-pitched voice became lower. With the exception of a few pubic hairs, the alopecia persisted. The skin changed to a pinker, healthier hue but did not lose its grossly abnormal characteristics.

Four months after the studies presented in figure 5 had been terminated, the patient commenced to have coronary heart disease, as evidenced by attacks of dyspnea and epigastric pain. Orthopnea gradually developed. At 7½ years of age he died, shortly after the onset of an acute cardiac episode consistent with a coronary thrombosis.

A postmortem examination was performed by Dr. B. Castleman and Dr. J. Tannheimer twelve hours after death. The following diagnoses were made:

Progeria
Coronary sclerosis, severe, with probable occlusions
Myocardial infarction, recent and old
Infarction of the left parietal lobe of brain, slight
Subdural hematoma
Arteriosclerosis, severe, generalized
Pulmonary edema and congestion
Meckel's diverticulum, small
Osteomalacia with fishmouth deformity of veretebral column
Postpuberal prostate

It was not possible to explain the clinical characteristics or metabolic features by any of the autopsy observations. With particular respect to the metabolic studies, it was of interest that there was a small amount of fat in the omentum, the mesentery and the perirenal tissue. The skin was largely devoid of fat except over the pubic region. The thyroid weighed only 6 to 8 Gm. The cells of the gland were cuboidal to columnar, and in several places there appeared to be hyperplasia with papillary invaginations. There was almost complete absence of colloid. There was no lymphoid infiltration. The appearance of the gland did not suggest the primary hyperplasia of exophthalmic goiter. Presumably the changes noted could be attributed to the thiouracil and possibly in part to the testosterone therapy. The latter therapy appeared to provide an adequate explanation for the development of the prostate gland.

The complete report of the postmortem examination is given in the appendix.

Papanicolaou, G. N., and Falk, E. A.: General cular Hypertrophy Induced by Androgenic Hor- , Science **87**:238, 1938.

GENERAL COMMENT

Data have been presented which tend to rule out hyperthyroidism as a cause for the hypermetabolism. In this connection, it is also of interest that the energy metabolism, as measured by the basal metabolic rate and the insensible weight loss, did not fall below normal limits even when the protein-bound serum iodine had fallen to very low values under thiouracil therapy. This suggests that some factor or factors other than thyroid were responsible for the excessive production of energy. Unfortunately, the nature of these factors remains for the time being a mystery. What relation they bear to the arteriosclerosis and the other bodily changes also falls into the sphere of pure speculation.

The development of dwarfing, skeletal changes, loss of subcutaneous tissue and arteriosclerosis in a progeric patient is a vigorous challenge to the clinical investigator. Though these studies have not solved the problem, they indicate that an excessive total energy output may be a characteristic of the disease. In this respect it is of interest that another progeric boy, aged 3 (fig. 7) was found to be ingesting approximately 105 calories per kilogram of body weight in his daily diet. Like the patient described in this paper, he also was unable to gain weight even on this large intake. Also, as with this patient, it has been difficult to induce him to eat more calories without prompting nausea and vomiting.

In attempting to explain the extreme loss of subcutaneous tissue in these patients, one is reminded of the numerous misleading efforts which have been made in the past to account for the opposite condition, obesity. It now seems certain that all obesity is due fundamentally to a positive caloric balance.[25] That is, obesity develops when the caloric intake of a person exceeds his requirements for energy metabolism and protein anabolism. The foregoing observations on these progeric children are equally in keeping with the fundamental laws of thermodynamics. In other words, it seems probable that the losses of subcutaneous tissue were due basically to a slight caloric deficit over a period of years. The deficit probably developed because of an elevated expenditure of energy of unknown cause. The patients were apparently unable to overcome this deficit by eating more calories. Hence, as has been shown for a person receiving an inadequate caloric intake,[17] the major endogenous source of the required calories is body fat.

25. Conn, J. W.: Obesity: II. Etiological Aspects, Physiol. Rev. **24**:31, 1944.

These ideas may be expressed diagrammatically, as in figure 8. Section *A* portrays conditions pertaining in the normally gr child. Here the caloric intake exceeds the c output, and a surplus is left over for the acc lation of body fat and for protein anab under the influence of growth hormones. conditions of section *B* are postulated fo progeric patient described here during the p

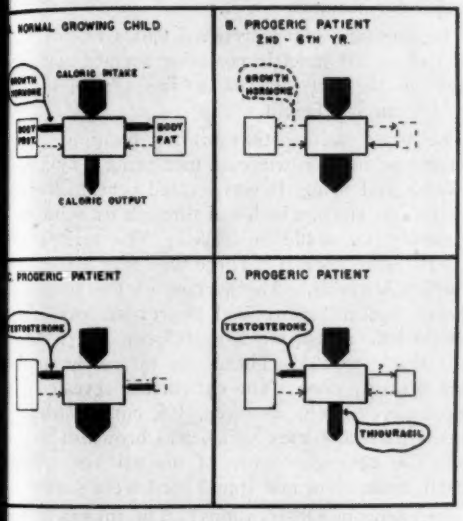
Fig. 7.—Appearance of another boy with proge years old. This patient had essentially the same hi and clinical features as the patient of figures 1 Note that he still has some subcutaneous tissue.

from 2 to 6 years of age, when most of subcutaneous fat vanished. The caloric in is slightly less than the caloric output, e because the intake is too small or the ou much too large. The consequent caloric de is met by the combustion of stores of body Because of the caloric deficit or because of s other disturbance, there is a deficiency of gr (protein anabolic) hormones. Lacking t

nones, the patient fails to anabolize protein e (that is, to grow) at a normal rate. sequently, he becomes both thin and dwarfed. vever, he is capable of growth, for when the th-promoting substance, testosterone, is bited there is considerable protein anabolism tion *C*). Yet, this anabolism of protein re- s the calories from food available for energy bolism. In the absence of a reduction of energy requirements, this deficit has to be good by an increase in combustion of body Finally, by artificially lowering the energy ut with the aid of thiouracil (section *D*), normal relations of section *A* are approxi- ed.

SUMMARY AND CONCLUSION

7½ year old boy with typical progeria was ied. The life history and the clinical and



g. 8.—Diagrammatic interpretation of metabolic ob- ations on the progeric patient. The caloric intake the normal child is based on the assumption that diet is well balanced.

mortem studies failed to explain the unique earance, the dwarfing and the loss of sub- neous tissue characteristic of this disease.

etabolic studies revealed that the patient in- ed and assimilated a quantity of food ade- e for the maintenance and growth of normal ldren of similar body weight. It appeared, vever, that all the calories in the diet were to meet the basal and intermediary require- ts of energy metabolism, thus leaving no due for growth or for the accumulation of utaneous fat. Under the influence of tes- erone therapy the patient gained a greater ght of musculature, according to the data on ogen and potassium balance, than he gained otal body weight. This was interpreted to mean that he had burned a significant amount of stored body fat to pay for the caloric deficit incurred by building muscle. The final studies showed that the patient could be made to gain by reducing the energy output with the aid of thiouracil.

It is concluded, therefore, that this patient with progeria was suffering from a metabolic disturbance which was characterized chiefly by an excessive utilization of calories for energy metabolism and which did not appear to be due to hyperthyroidism as it is ordinarily encountered in children. As a consequence of the hypermetabolism, even when the patient was assimilating a good diet, few if any calories were available for growth. It may be profitable to search for a similar disturbance in other types of patients who fail to gain or grow.

APPENDIX

The necropsy was performed in the Department of Pathology at the Massachusetts General Hospital. Dr. B. Castleman reviewed and edited the report of the pathologic observations.

Gross Examination.—Most of the salient features of the external appearance have already been mentioned in the report of the clinical examination. A few additional details deserve mention. The submaxillary and sublingual salivary glands stood out clearly and were firm and unattached to the skin. The skeletal muscles of the body were well developed, firm and dark reddish brown and gave to the extremities the proportions of an adult body. The small joints of the hands and feet, the wrists, elbows and ankles showed pronounced changes reminiscent of advanced hypertrophic arthritis of old age. There were faint suggestions of Heberden's nodes on the third and fourth fingers bilaterally. The nails were thin, straight and of normal proportions. The penis was large, measuring about 5 cm. in length and 2 cm. in diameter. The testes weighed 4.5 and 5.5 Gm. and were retained in the proportionately developed scrotum.

Peritoneal Cavity: The viscera had normal relations but appeared crowded in too small a cavity. There was a small quantity of yellow fat in the omentum, mesenteries and perirenal tissue.

Intestines: There was a small Meckel diverticulum arising from the ileum 50 cm. from the ileocecal valve.

Thyroid: The thyroid gland weighed 6.8 Gm., was of the usual shape and was moderately firm and dry and of a reddish gray color.

Parathyroid Glands: None of the parathyroid glands were definitely identified despite thorough search.

Heart: The heart weighed 150 Gm. The transverse diameter was 11.5 cm. The pericardium was normal and contained 15 cc. of a clear, pale amber fluid. There was no epicardial fat. There was congestion of the superficial vessels, especially over the apex of the heart. Most of the myocardium was of a uniform red-brown color and of moderately soft consistency. Except for the area to be specifically described, the wall of the left ventricle measured about 1.3 cm. in thickness, while that of the right ventricle was 0.3 to 0.4 cm. thick. Over the central portion of the interventricular septum there was a sharply defined area, 4 to 5 cm. in diameter, wherein the myocardium was softer and showed

numerous linear and round hemorrhages. Another area of softness, 1.5 cm. in diameter, was located on the anterior surface of the left ventricle near the apex. The thickness of the muscle in this region was reduced to 0.9 cm. With one exception, the endocardium was smooth, glistening and gray. It showed red-gray mottling on the left ventricular side of the interventricular septum adjacent to the hemorrhagic area just mentioned.

The mitral valve measured 6.2 cm. in circumference. The leaflets were opaque and dusky gray. Small yellow plaques were seen on the aortic leaflet, and there were small foci of calcification along the annulus fibrosus. The free edges were fairly thick but were smooth. The chordae tendineae were long and thin. The papillae and trabeculae carneae were fairly prominent. The aortic valve measured 4.2 cm. in circumference. The cusps were thin and were not adherent to each other. The entire wall of the sinuses of Valsalva were covered with atheromatous plaques. The circumference of the tricuspid valve was 7.5 cm., and that of the pulmonary valve was 4.5 cm. Both of these valves were normal in appearance.

Coronary Arteries: The ostium of the right coronary artery was narrowed to 1 mm. at its orifice by an aortic atheromatous plaque. This plaque extended for 1 or 2 mm. into the coronary artery. From that point onward the artery was soft and widely patent, except for a few small atheromatous plaques which narrowed the lumen locally. The ostium of the left coronary artery was similarly narrowed to 1.5 mm. The anterior descending portion of the left coronary artery was strikingly narrowed by a calcified and thickened intima. For a distance of 2 cm. the opening was of pinpoint caliber. In a few spots the lumen may have been completely occluded. The largest septal branch of the anterior descending artery arose from this narrow portion. It was likewise of reduced caliber, and that portion which was within the interventricular septum was probably completely occluded. There was no evidence of recent thrombosis. The left circumflex artery was widely patent and presented only a few noncalcified atheromatous plaques.

Aorta: The circumference of the aorta was 3.6 cm. in the ascending portion, 3.5 cm. at the arch and at the level of the diaphragm, 2.5 cm. at the origin of the renal arteries and 1.5 cm. at the level of the inferior mesenteric artery. Longitudinal and transverse resilience was well preserved. The ascending aorta was free from arteriosclerotic changes except for a few small atheromatous plaques just above the valve in the sinuses of Valsalva. The arch and descending aorta, however, had many soft, yellow, noncalcified intimal plaques measuring up to 3 mm. in thickness. Most of these were oval and were alined parallel with the lumen. They extended into the iliac and femoral arteries. The pulmonary artery and the vanae cavae were normal.

Skeleton and Bone Marrow: The medullas of the femur, tibia and fibula were filled with thick red marrow. The cortex of these bones was hard and measured 2 to 3 mm. in thickness. The vertebrae were moderately soft and were not densely calcified, though the trabeculae of the medullas were fairly coarse and strong. The marrow here was red and ample. The vertebral bodies were lenticular, with strongly arched biconvex surfaces which accommodated biconcave disks. These were narrowed at their centers, with an absence of nuclear pulp, so that the cartilaginous surfaces were nearly or directly in contact with each other. On the anterior and lateral surfaces of the spinal column, however, the intervertebral disks were as wide as or wider than the exposed surfaces of the vertebrae. The vertical bodies w oval, with a transverse diameter considerably gre than the anteroposterior diameter.

Head: The calvarium was thin and in most a was 2 mm. or less in thickness. The bone was l but not brittle and bent readily. In the vertex of cranium was a 3 by 5 cm. oval area where densely packed, irregular, 3 to 5 mm. long bony spic projected into a soft, dark, reddish blue pad of gran tissue which lay on the dura above and lateral to normal superior longitudinal sinus. There was no cernible distinction between inner and outer tables. base of the cranium was everywhere deeply impre by the configurations of the cerebral gyri. The sup orbital plates were especially deeply impressed. cranial cavity was strikingly spherical. The bounda between the fossae were leveled and rounded, and appeared that the lateral walls of the cranium m have been forced outward. The meninges were nor There were a few atheromatous plaques in the int of the basilar, internal carotid and cerebral arter The venous sinuses were patent. However, the late sinuses did not follow their normal course but for straight, direct channels from the confluens sinuum the jugular foramen.

The pituitary gland weighed 0.61 Gm. It was o and had an asymmetric posterior surface, with a sl bulge on the left side measuring 4 mm. in diame and 1.5 mm. in height.

The brain was sectioned after fixation. The c revealed an oval brown area, measuring 3 by 5 by 1 c granular and firm. It was located beneath the super longitudinal sinus, which ran through its substance. communication could be traced. The main arteries the base were normal. There was only a slight amo of arteriosclerosis. The surface of the cerebral he spheres had a longitudinal depression over the r parietal lobe measuring 3 by 0.5 cm. and with its a transversely placed. There was no cerebellar or u poral pressure cone. The cut surface revealed no gr abnormality except an area, 0.5 cm. in diameter, the left parietal cortex which was brownish and irre lar. The ventricles were of normal size. The ce bellum, brain stem and spinal cord were normal.

Miscellaneous Observations: The thymus (9.5 Gm the liver (930 Gm.), the spleen (100 Gm.), the pancr (70 Gm.), the adrenals (2.3 and 2.5 Gm.), the k neys (combined 190 Gm.), the prostate (2 by 1.5 1.5 cm.), the moderate-sized seminal vesicles, the te (4.5 and 5.5 Gm.), the gastrointestinal tract, the mes teric and retroperitoneal lymph nodes, the respirat tract (except for pulmonary congestion and edem the air sinuses and middle ears, the mediastinum, gallbladder, the ureters, the bladder and the periphe nerves revealed nothing remarkable.

NOTEWORTHY MICROSCOPIC OBSERVATIONS

Heart: The epicardium was thickened, fibrous a vascular, wtih a moderate amount of lymphocytic infilt tion. The arteries, both in the epicardium and in t myocardium, showed extensive arteriosclerotic chan In and around the adventitia was deposited much fibr tissue, some of which had undergone amorphous hyal zation. The intima showed extensive areas of moder to pronounced thickening, mostly in the form of arter sclerotic plaques with few to many cellular eleme Most of these plaques were loose and cystic in str ture. Some contained large numbers of very large mo nuclear foam cells. The plaques were entirely wi the inner elastic membrane, which was usually in

th the plaques. The central portion of thick, in- plaques showed hyalinization and some deposition lcium. The intimal lining was smooth, and no nbi were seen. The lumen was definitely narrowed, g only a slitlike opening (fig. 9). The endo- um was uniformly thickened and fibrous. The ardium showed extensive change. Throughout were areas showing all stages of myocardial infarction, ding hemorrhage, destruction of muscle, granula- fibrosis and hyaline degeneration of scar tissue. interventricular septum showed an extensive infarct osed predominantly of fibroblasts, monocytes, hocytes and an occasional polymorphonuclear cell. infarct was probably of two to three weeks' dura- and was superimposed on several small focal areas farction in various stages of healing and scarring. left ventricular wall showed small areas of de- ration of muscle fiber. A portion of the major

g. 9.—Arteriosclerosis of coronary artery. Note the lumen is narrowed so that only a slitlike open- remains.

la showed recent infarction with hemorrhage, poly- honuclear infiltration and acute muscular degenera- The overlying endocardium was thickened by us tissue, and under the endocardium was a thick in which muscle fibers were replaced by large and foamy phagocytes. The muscle immediately ent showed waxy degeneration.

rta: The aorta showed intimal plaques which the same loose, cystic and haphazard structure and y macrophages as the intimal plaques of the cor- y arteries.

dneys: Arteries and capillaries in the kidneys everywhere congested with blood. The glomerular were congested but were otherwise normal. The arterioles showed slight medial hypertrophy but vidence of intimal hyalinization.

Liver: The liver showed extreme congestion with pronounced narrowing and destruction of cords. Near the centers of the lobules what few liver cells remained were vacuolated and foamy and contained many pigment granules. Periarterial fibrous tissue was moderately increased and partially hyalinized.

Spleen: The pulp was heavily loaded with red blood cells. The small arteries had thickened walls. The intima was irregularly thickened and showed hyaline change and roughened, frayed intimal lining. Malpighian corpuscles were fairly numerous.

Mesenteric Vessels: The mesenteric vessels showed the same arteriosclerotic vascular changes described in the coronary arteries.

Adrenals: The adrenal glands showed the same degree of vascular change as the coronary arteries. No other abnormal features were seen.

Pancreas: The pancreas showed postmortem change. Thickening of all layers was prominent in the larger vessels.

Thyroid: The cells of the thyroid were cuboidal to columnar, and in several places there seemed to be hyperplasia with papillary invaginations. There was almost complete absence of colloid, but where colloid was present there was suggestive scalloping. There was no lymphoid infiltration. The appearance did not suggest the primary hyperplasia of exophthalmic goiter.

Thymus: A large amount of thymic tissue remained. The complete absence of adipose tissue was a striking feature. Hassall's corpuscles were numerous and small. There was no evidence of hyperplasia. Germinal centers were absent.

Skin: In a sample of skin from the pubic area, the epidermis appeared normal; hair follicles and sweat glands were present, and a normal amount of subcutaneous adipose tissue was seen. In a specimen from the abdominal wall, the epidermis was normal, as were the sweat glands, but hair follicles were absent. A fairly thick layer of fibrous and dense areolar tissue filled the subcutaneous area. Practically no fat cells were present here. A specimen from the scalp revealed the skin in this area to be thin. Few hair follicles were present. The subcutaneous tissue was thin and contained many large veins. No fat cells were seen.

Prostate: The tubules of the prostate were lined with columnar epithelium and in many places showed papillary folding of the epithelium. This observation is consistent with postpuberal prostatic development. (The patient had been receiving testosterone.)

Testes: The seminiferous tubules were small and contained Sertoli cells and a fair number of early forms in the spermatocyogenic series. There was no evidence of spermatogenesis. Cells of Leydig were not increased in number.

Brain: There was an area of hemorrhage immediately underlying the dura. Under this area there was a broad band of nucleated cells. There were many giant macrophages in this area. Immediately outside the adventitia of the capillaries and arterioles there was some fuzzy noncellular material. The capillaries and arterioles stood out prominently and had a well demarcated perivascular space. Unfortunately, the sections of the pituitary were not available.

Dr. Max Gilbert of the Schering Corporation provided the methyl testosterone, the testosterone propionate and the estradiol benzoate used in these studies.

Miss S. Wells, B.S., M.S., and Miss M. Macauley, R.N., assisted in the dietary management and the nursing care of the patient.

PYODERMIC MYIASIS IN CHILDREN

OBSERVATIONS WITH SPECIAL REFERENCE TO TÓRSALO

LEON GOLDMAN, M.D.
CINCINNATI

In some sections of tropical America one of the common forms of acute cutaneous lesions in children is cutaneous myiasis. In the United States, cutaneous myiasis in children occurs usually, according to my experiences, as a secondary infestation in chronic ulcerative cutaneous lesions, especially draining wounds about edge of a hip spica used as a basis for a pl cast. Creeping eruption, a serpiginous tunn of the skin, caused in some instances by larvae, has been observed mainly in adults may be found also in children in Florida Texas.

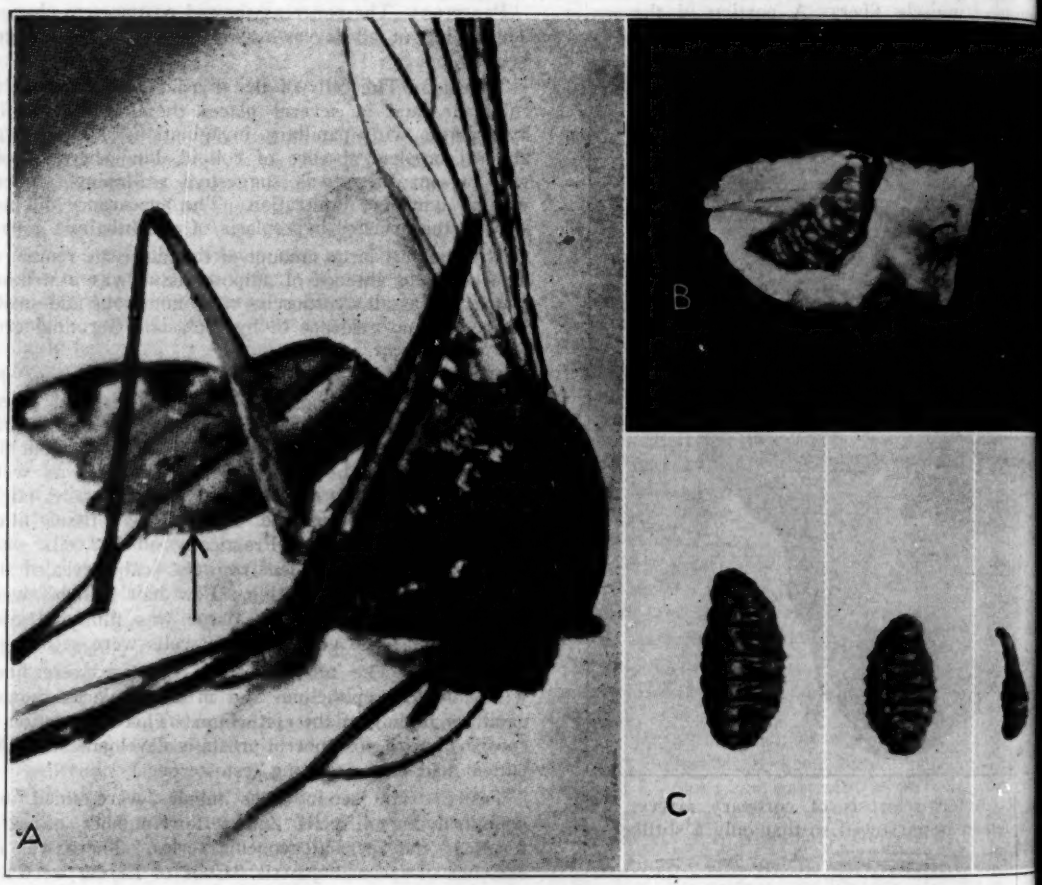


Fig. 1.—*A*, Aedes angustivittatus of Puntarenas, Costa Rica, with eggs of Dermatobia hominis adherent abdomen (Peña Chavarría and Kumm). *B*, section of skin showing cavity of pyodermic myiasis with placed in position. *C*, group of larval forms of Dermatobia hominis.

I observed primary pyodermic myiasis in C Rica. This cutaneous myiasis is called *tórsa* Costa Rica, *nuche* in Colombia, *berne* in Br and *gusano de monte* in Venezuela. The ease in Costa Rica has been studied extens

Work was done under a grant from the John R. and Helen Markle Foundation through the Association of American Medical Colleges, Dr. Henry E. Meleney, Chairman.

From the Department of Dermatology and Syphilology of the University of Cincinnati College of Medicine and the San Juan de Dios Hospital, San José, Costa Rica, Dr. Antonio Peña Chavarría, Director.

Peña Chavarría [1] and his associates. The fly erned in this form of myiasis in Costa Rica e bot or warble fly, Dermatobia hominis. detailed description of the fly and its larval s may be found in standard texts on sitology.[2]

. 2.—Infant with congenital syphilis complicated odermic myiasis about eye and forehead. Lesions med at autopsy.

he eggs of the D. hominis adhere to the of a mosquito. Two forms of Aedes have found in Costa Rica as carriers of these , Aedes angustivittatus and Aedes serratus. ropical America, other insects besides the quito may serve as egg carriers. The larvae e out of the egg membrane when the quito vector settles on the skin. The larvae r the skin through the puncture wound made he mosquito. In the skin the larvae develop, iring from forty-six days to "as long as two a half or three months." [1] Then they crawl of the skin and fall on the ground to pupate. ccording to Costa,[3] any part of the skin may nfested by the larvae of D. hominis. In the pital San Juan de Dios in San José, Costa , Peña Chavarría noted that 112 persons ght hospitalization for cutaneous myiasis from 8 to 1937. The majority of their lesions eared first on the head, next on the face. quently the lesions are multiple, especially in the furuncular types, as observed in Brazil by Costa. In some instances the larvae may migrate a short distance from the area in which they enter originally.

To persons who are not familiar with this disease, the lesions appear as indolent pustules or furuncles. If one watches the white cap or head of the lesion closely, however, one can detect slight movement. Movements of the larvae within their canals also produce considerable pain and discomfort. Because of the irritation and secondary infection from the parasites, the lesions may become moderately large. The secondary infection may involve also the adjacent cutaneous surface and produce extensive ulceration. One lesion removed from an adult at an autopsy at San Juan de Dios Hospital by Dr. Nettleship revealed a cavity approximately 2.5 cm. in diameter and containing bits of necrotic fragments of the parasite.

Microscopic examination of a myiasis cavity showed some degree of marginal acanthosis about the opening. The lining was made up of fragmented poorly staining collagen fibers studded with areas of necrosis, of perivascular, polymorphonuclear and lymphocytic reactions and also of periglandular inflammatory cell groups. The cavity involved the fat tissue. Portions of larvae of D. hominis were recognized in the purulent debris in the cavity. There was no unusual tissue eosinophilia about this area.

Fig. 3.—Extensive scarring which may develop from a pyodermic myiasis of the face.

Lesions of pyodermic myiasis should be recognized early to avoid increase in size and the aggravating effect of secondary pyogenic infection. With a fine forceps the larva may be picked out, and antiseptic mixtures may be used

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. Craig, C. F., and Faust, E. C.: Clinical Para- ogy, ed. 3, Philadelphia, Lea & Febiger, 1943, p. 600.

. Costa, O. G.: Furuncular Myiasis, Arch. Dermat. yph. **50**:36 (July) 1944.

in the cavity after irrigation. Concomitant avitaminosis should also be treated to accelerate the healing process. If necessary, incision and drainage may be done.

To prevent lesions of cutaneous myiasis, attempts should be made to keep the insect vectors from the skin. This is difficult with native groups. Breeding areas of the flies and the carriers of their eggs should receive attention also and should be treated with the modern methods for the chemical control of insects.

SUMMARY

A common form of cutaneous myiasis served in the American tropics, especially children, is of the pyodermic type, with pust furuncles and even carbuncles as varying deg of secondary infection about the larval for usually of D. hominis.

Dr. Peña Chavarría and his staff placed the pati and material at my disposal.

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SULFATHIAZOLE OINTMENT FOR PREVENTION AND TREATMENT OF PYODERMAS OF NEWBORN INFANTS

RESULTS OBTAINED WITH FIVE PER CENT SULFATHIAZOLE IN AN OIL IN WATER TYPE EMULSION BASE

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This is a condensed preliminary report of two rs' experience with an ointment consisting of er cent sulfathiazole in an oil in water type lsion base used as a prophylaxis against etigo and other pyodermas for 3,205 newborn nts. A report of its therapeutic use also is uded.

We were led to employ this preparation use our results with all previous procedures preparations had been unsatisfactory and use Pillsbury, of the dermatologic depart- t of the University of Pennsylvania, recom- ded this particular preparation as highly ient and unlikely to produce toxic effects.

Since 1941, when Hawking [1] and Jervey [2] orted on the local use of sulfonamide com- nds, many papers have appeared which testify the effectiveness of these drugs. Shaffer [3] Pillsbury [4] have published excellent reviews this material. These papers indicate that fathiazole ointments, among other sulfonamide pounds, are very effective against pyoderma, the concentration must be at least 5 per cent that higher concentrations of sulfathiazole no better. Pillsbury, Shaffer and Nichols [5] e shown that the use of an oil in water type lsion base definitely enhances the degerming ct of the sulfathiazole ointment and makes the e much easier to apply and to remove. Furthermore, there is little local cutaneous irritation and little absorption of sulfathiazole from normal skin.

The ointment produced by the incorporation of 5 per cent sulfathiazole in an emulsion of oil and water is a smooth, white, creamy one. The preparation used by us was prepared according to the following formula:

Sulfathiazole	5%
Sodium lauryl sulfate	1%
Stearyl alcohol	10%
Cetyl alcohol	3%
Spermaceti	10%
Glycerin	10%
Water	61%

PRACTICAL EXPERIENCE WITH CARE OF THE SKIN OF NEWBORN INFANTS

Following is the routine which has been used in the nurseries for newborn infants at Long Island College Hospital since August 1942. Immediately after the newborn infant has been cleansed with sterile corn oil, it is anointed over all with 15 Gm. of the 5 per cent sulfathiazole preparation. After twelve hours, a thorough tub bath is given. Unless pyoderma develops, no further inunctions are given. If it does develop, the affected infant or infants are isolated, the individual lesions are opened under 70 per cent alcohol and frequently repeated applications of the special ointment are made. The nursery is closed to all new admissions, and each infant in it is again anointed with 15 Gm. of the special 5 per cent sulfathiazole ointment.

TABLE 1.—*Routine Care of Skin of Newborn Infants at Long Island College Hospital*

1. Cleanse skin with sterile corn oil.
2. Anoint entire body with 15 Gm. of 5 per cent sulfathiazole ointment (in an oil and water emulsion base).
3. After twelve hours give soap and water bath.
4. Isolate any infant in whom pyoderma develops, and close the nursery to new admissions.
5. Reanoint all exposed infants with 15 Gm. of 5 per cent sulfathiazole ointment (emulsion base).
6. Treat pyoderma by emptying pustules under 70 per cent alcohol and frequent local applications of 5 per cent sulfathiazole ointment (emulsion base).

Presented at the meeting of the American Pediatric iety, Atlantic City, N. J., Sept. 26, 1944.

From the Departments of Pediatrics and the Service Dr. Alfred C. Beck, Professor of Obstetrics, Long nd College of Medicine, Long Island College Hos- l Division.

1. Hawking, F.: Methods for the Local Application Sulfanilamide, Brit. M. J. **2**:685-686 (Nov. 15) 1941.
2. Jervey, W. St. J.: The Local Use of Sulfon- des, South. Med. & Surg. **103**:643-645 (Dec.) 1941.
3. Shaffer, B.: The Use of Sulfonamide Compounds Dermatology, Connecticut M. J. **7**:237-243 (April) 3.
4. Pillsbury, D. M.: Sulfonamides in Dermatology, J. Dermat. **56**:68-80 (March-April) 1944.
5. Pillsbury, D. M.; Shaffer, B., and Nichols, A. C.: terial Flora of Normal Skin: A Study of the Effect Sulfathiazole and Some Ointment Bases, J. Invest. rmat. **5**:371-379 (Dec.) 1942.

If new instances of the disease occur, the procedure is repeated.

During the years which preceded the adoption of this nursery routine, we employed two other routines, with the customary poor results. From 1930 to 1940, infants in whom pyoderma developed were isolated and treated with various remedies then current; the nurseries were closed to new admissions, and the newly infected infants were isolated. Of the 10,534 infants born at Long Island College Hospital during those ten years, pyoderma developed in 130 (table 2). The outbreaks were multiple and apparently self limited. There was much variation in severity, as is the common experience.

Because of the frequency and potential danger of pyoderma we were on the lookout for and were willing to try the various new agents as they were suggested. Therefore, in 1940 we anointed each newborn infant with 15 Gm. of 2 per cent ammoniated mercury ointment after the baby had been cleansed with sterile corn oil. Six hours later, residual ointment was removed by means of a soap and water bath. If an outbreak of pyoderma occurred, the affected infant or infants were isolated and treated with 5 per cent sulfathiazole water-soluble ointment. The nursery or nurseries were closed to new admissions. All infants exposed to pyoderma were reanointed with 15 Gm. of 2 per cent ammoniated mercury ointment. The soap and water bath and removal of ointment followed in six hours. The procedure was repeated if there were multiple exposures to pustular infection during the infants' stay in the hospital.

TABLE 2.—*Comparison of Three Routines for Care of the Skin of Newborn Infants*

Date / Method	Infants: Total Number	Infants: No. with Pyoderma
A. 1930-1940	10,534	130
1. Isolation 2. Closure of nursery 3. Local treatment (various)		
B. 1940-1942	3,064	35
1. Inunction with 2 per cent ammoniated mercury ointment 2. Isolation 3. Reinunction of contacts with 2 per cent ammoniated mercury ointment 4. Closure of nursery 5. Local treatment with 5 per cent sulfathiazole ointment (emulsion base)		
C. 1942-1944	3,205	4
1. Inunction with 5 per cent sulfathiazole ointment (emulsion base) 2. Isolation 3. Reinunction with 5 per cent sulfathiazole ointment (emulsion base) 4. Closure of nursery 5. Local treatment with 5 per cent sulfathiazole ointment (emulsion base)		

During the two years 1940 to 1942, there w 3,064 infants born at Long Island College H pital and so treated; in 35 of them pyode developed. The outbreaks were multiple, usual, and were of varying severity.

The customary treatment of acute erupt included evacuation of pustules under 70 per alcohol and application of various local age all of which were unsatisfactory. With change to 5 per cent sulfathiazole ointment results greatly improved and they became better after sulfathiazole was available in emulsion base. Spread of infection was trolled; lesions healed quickly and toxic eff both local and general, were negligible. In trast to this experience, ammoniated mer ointment seldom limited spread or aided heal there was much dermatitis venenata, and ointment was difficult and disagreeable to ha In fact, just before we abandoned its use, in 1942, we observed rapid spread of impetigo f an infected infant to 4 others, even though had just been reanointed with 2 per ammoniated mercury ointment.

From August 1942 to August 1944, anointed 3,205 infants with 5 per cent su thiazole ointment in an emulsion base, and the time of writing have had 4 sporadic insta of pustular infection among those anointed, no spread. More striking still was an accide experience. A severely asphyxiated infant ceived vigorous treatment for some six h before admission to the nursery. Inadverte the inunction with sulfathiazole on admission omitted. Within forty-eight hours a widesp bullous impetigo developed. The infant immediately isolated and treated as previou described: The neighboring 15 infants who w thus exposed were reanointed with 15 Gm. sulfathiazole ointment in an emulsion base their nursery closed to new admissions. No eruptions developed in that nursery or in adjoining nursery. The infected infant recov in forty-eight hours.

CLINICAL AND LABORATORY DATA ON POSSIBLE TOXIC EFFECTS OR SENSITIZATION

After it became apparent that our clin results with this regimen were far better than we had had with others, data were colle which might indicate whether there were l or general toxic effects or whether sensitiza to sulfonamide compounds might have b initiated.

Since December 1943 we have carefully served 824 infants who had been anointed w 5 per cent sulfathiazole ointment in an emul

to study the incidence of cutaneous irrita-
. Only 17 infants (2 per cent) had any
This was usually a moderate, generally
ibuted maculopapular rash which dis-
ared in about forty-eight hours.

ur studies of the blood sulfathiazole levels
hese infants have corroborated Pillsbury's
ment that the concentration of sulfathiazole
e blood is not significantly elevated; nor was
important alteration in the blood or urine
le 3).

lood sulfathiazole levels were estimated
nty-eight times by the micromethod described
orgensen.[6] The levels were taken at various
s after inunction, ranging from three hours
ne hundred and ninety-three hours. The
s varied between a trace and 1.7 mg. per
lred cubic centimeters; the commonest level
rved was 0.5 mg. per hundred cubic centi-
ers. By this method these levels are con-
red insignificant.

omplete blood counts were made for 92 in-
s at various times after inunction. The red
d cells varied between 6,510,000 and
0,000; the hemoglobin content, between 16
13 Gm., and the white blood cells, between
00 and 11,000. There was no interesting
nge in the types of cells observed or in the
erential count. Forty-nine random urinalyses
losed no abnormalities.

he subsequent admission to the hospital of
of the 3,205 infants who had been anointed
the special 5 per cent sulfathiazole ointment
birth, for illnesses which required oral or
nteral administration of sulfonamide com-
nds, offered a remarkable opportunity to

LE 3.—*Laboratory Observations on Newborn Infants After Inunction with 15 Gm. of 5 per Cent Sulfathiazole Ointment (Emulsion Base)*

	Number of Estimations	Results
d sulfathiazole levels	78	Trace to 1.7 mg. per 100 cc.
d counts	92	Red blood cells 6,500,000 to 4,200,000; hemoglobin content 16 to 13 Gm.; white blood cells 28,000 to 11,000
lyses	49	No change

ermine whether or not this group had become
sitive to these compounds (table 4).

he illnesses for which sulfonamide com-
nds subsequently were administered were
dominantly of the respiratory tract. Forty-
of the 49 infants were so afflicted, most of

. Jorgensen, G. M.: Simplified Micromethod for
d Sulfonamide Determination; J. Lab. & Clin.
. 27:1355-1357 (July) 1942.

them having pneumonia. Meningitis and septicemia were included. All these infants received full doses of sulfonamide compounds, and to 4 of them high doses were given for more than twenty days. The sulfonamide compounds used in treating these 49 infants were sulfathiazole for 43 of the 49 infants, sulfadiazine for 4 infants and

TABLE 4.—*Results in Treatment of 49 Infants Anointed at Birth with 5 per Cent Sulfathiazole Ointment (Emulsion Base) and Given Sulfonamide Compounds on a Later Admission to the Hospital* *

	No. of Infants
Diagnosis	
Diseases of respiratory tract (pneumonia 26)	39
Meningitis	1
Osteomyelitis	2
Miscellaneous	7
Total	49
Drug used	
Sulfathiazole	43
Sulfadiazine	4
Succinylsulfathiazole	2
Total	49
Interval in months between birth and treatment	
0 to 1	12
1 to 2	7
2 to 3	5
3 to 4	6
4 to 5	5
5 to 6	3
6 to 7	3
7 to 8	2
8 to 9	1
9 to 10	2
10 to 11	2
11 to 12	1
Total	49

* There were no toxic manifestations.

succinylsulfathiazole for 2 infants. Twelve of these infants received sulfonamide compounds orally before they were 1 month old. Table 4 shows the number of infants who received full doses of sulfonamide compounds at various intervals after the inunction at birth. These preliminary observations cover only twelve months after birth. Information was sought on the incidence of rashes, gastrointestinal disturbances, drug fever, renal disturbances and alterations in blood count which might be attributable to sulfonamide compounds. In none of these 49 patients was there evidence of either local or general sensitization to these compounds.

SUMMARY

To summarize, we have so far anointed 3,205 infants just after birth, with 15 Gm. of 5 per cent sulfathiazole in an emulsion ointment base, in an attempt to prevent pustular infections. If the infants were exposed, we have reanointed them with this preparation, closed the nursery, and treated any infant with pyoderma by evacuating pustules under 70 per cent alcohol, followed by

frequent local application of 5 per cent sulfathiazole water-soluble ointment.

The results have been excellent. From August 1942 to August 1944, there have been only 4 sporadic cases of pyoderma in 3,205 newborn infants, without spread to neighboring infants in the same nursery or to those in adjacent nurseries. The blood sulfathiazole levels, blood counts and results of urinalyses were not significantly altered.

Forty-nine of the 3,205 infants who had had prophylactic inunction with 5 per cent sulfathiazole ointment in an emulsion base were readmitted for serious illnesses which required full dosages of sulfonamide compounds. In 43 instances the sulfonamide compound employed was sulfathiazole. No instance of sensitization to sulfonamide compounds was encountered.

Admittedly, our short experience is insufficient to prove that this agent will always be equally effective and productive of no untoward results. However, according to present observations, the ointment has vastly aided in the prevention and improved the management of pustular infections in the nurseries for the newborn during th two years.

While most of these 3,205 infants apparen were protected by the application of sulfathiaz ointment immediately after birth, we do not w to convey the impression that all pyodermas due to infection acquired during the pass through the mother's birth canal. During period covered by this study our babies w discharged from the hospital between the seve and the tenth day after birth, because of shortage of maternity beds. Had they been k in the hospital for two weeks, as was our for custom, more sporadic infections might possi have occurred. Furthermore, the natural hist of pyoderma in infants is characterized periods of very low incidence even though special control measures are taken. Seve years' more observation, rather than the obs vation of larger numbers of cases, will show h helpful this new agent is as an adjunct to g nursery technic.

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Case Reports

OBSTRUCTIVE PULMONARY EMPHYSEMA ASSOCIATED WITH PNEUMONIA IN CHILDHOOD

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Regional obstructive pulmonary emphysema children following an acute infection of the per respiratory tract has only recently been cognized as a clinical entity. Benjamin and ilde [1] presented this subject for the first time, November 1939.

Recently 2 cases of pulmonary emphysema ere observed in the pediatric service of the enox Hill Hospital.

REPORT OF CASES

CASE 1.— S. S., a 6 week old girl, was admitted to the spital on May 26, 1943, with a history of irritability d frequent crying and with a temperature of 103 F. four days' duration. Two days prior to her admis- n the child began to cough and to have rapid res- ration. On the day of her admission she expectorated small amount of white sputum.

Examination of the child on her admission revealed at she was pale and acutely ill but not cyanotic. here was dulness to percussion over the entire right le of the chest, both anteriorly and posteriorly, with epitant rales and bronchial breathing over the entire ea. The left side of the chest was clear. The liver as palpable 2 to 3 fingerbreadths below the costal argin. The leukocyte count was 30,000 per cubic illimeter of blood, with 66 per cent polymorphonuclear ukocytes (34 per cent immature forms) and 34 per nt lymphocytes. The erythrocyte count was 2,000,000; e concentration of hemoglobin in the blood was 44 r cent, or 6.6 Gm. per hundred cubic centimeters. he patient's temperature was 103.6 F.

A diagnosis of pneumonia was made, and sulfadiazine erapy was instituted, 1½ grains per pound (0.2 Gm. r kilogram) of body weight in twenty-four hours. he child was placed in an oxygen tent. Transfusions 70 and 50 cc. of whole citrated blood were given on e second and third days respectively. The sputum owed pneumococci, but the organisms could not be ped, and none were recovered by a mouse inoculation. dministration of sulfadiazine was discontinued on the urth day, after a total of 27.5 grains (1.79 Gm.) had been given. The temperature remained normal. On the seventh day the temperature rose to 103 F., and the leukocyte count was 34,100 per cubic millimeter, with 82 per cent polymorphonuclear leukocytes (32 per cent immature forms), 16 per cent lymphocytes and 2 per cent monocytes. Sulfadiazine therapy was again given, and the temperature became normal on the ninth day. The child was discharged from the hospital on the sixteenth day with a normal temperature; her erythrocyte count was 3,500,000; the concentration of hemoglobin in the blood was 65 per cent (9.5 Gm. per hundred cubic centimeters of blood). After being discharged the child gained weight; at the time of writing she is asymptomatic and afebrile. The patch test for tuberculosis was negative.

CASE 2.—E. V., a 7 month old white boy, was admitted to the hospital on March 28, 1944, with a history of cough, fever and irritability of twenty-four hours' duration.

Examination revealed that the infant was acutely ill and had a temperature of 102.8 F. There was dulness to percussion at the apex of the left lung posteriorly, with crepitant rales. The right lung was clear. Both ear drums were injected. The leukocyte count was 12,000, with 56 per cent polymorphonuclear leukocytes (12 per cent immature forms) and 44 per cent lymphocytes. The erythrocyte count was 2,000,000, and the concentration of hemoglobin in the blood was 56 per cent, or 8.4 Gm. per hundred cubic centimeters.

Sulfadiazine therapy was instituted—1½ grains per pound (0.2 Gm. per kilogram) of body weight in twenty-four hours. The temperature became normal on the third day and remained so. Administration of sulfadiazine was discontinued on the sixth day, after a total of 75 grains (4.9 Gm.) had been given. Diplococcus pneumoniae type 14 was found in the sputum and was recovered by a mouse inoculation. A transfusion of 130 cc. of whole citrated blood was given on the ninth day. The child was discharged on his eighteenth day in the hospital, with an erythrocyte count of 3,500,000 and 71 per cent, or 10.6 Gm., of hemoglobin per hundred cubic centimeters.

These 2 cases fulfil the criteria for the diagnosis of obstructive pulmonary emphysema. In both cases the emphysema followed an acute infection of the upper respiratory tract. After resolution of the pneumonia the emphysematous area was demonstrated, and the characteristic roentgenographic picture, the absence of physical

From the Abraham Jacobi Division for Children of e Lenox Hill Hospital, service of Dr. Jerome S. eopold.

1. Benjamin, B., and Childe, A. E.: Localized Bul- us Emphysema Associated with Pneumonia in hildren, J. Pediat. **15**:621, 1939.

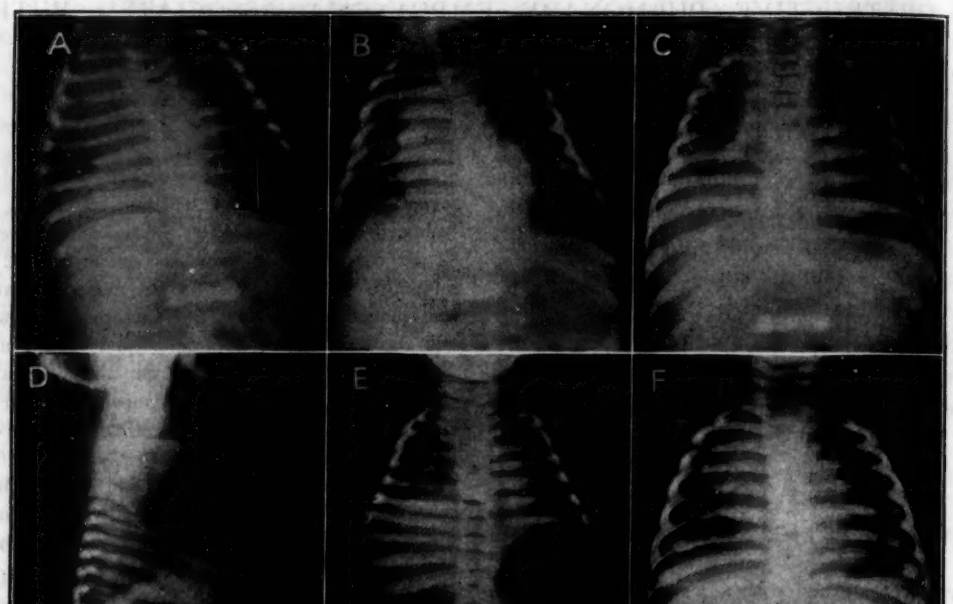

Fig. 1.—Chest of the patient in case 1. *A*, roentgenogram made on the day of her admission to the hos shows complete consolidation of the upper two thirds of the right lung. The remainder of the parenchyma of lung seems clear. *B*, a roentgenogram made on the seventh day shows an area of decreased density, measu 1.5 by 2.5 cm., in the lower portion of the consolidated upper lobe. *C* and *D*, roentgenograms made on the ninete day show clearing of the parenchyma of the lung on the right side. The cavity is larger than before, measuri by 3 cm. The cavity appears to be loculated, especially in the lateral view. *E*, a roentgenogram made on the thi sixth day shows that the right lung is clearing. The cavity is smaller, measuring 1.5 by 2.5 cm. *F*, a roentg gram made on the one hundred and twenty-sixth day shows that the cavity has disappeared. Increased densi present in the upper part of the right lung. The shadow may represent an area of atelectasis in upper lobe of right lung, the shadow of an enlarged thymus or a mediastinal mass. The child is asymptomatic, and no phys signs are found in this area.

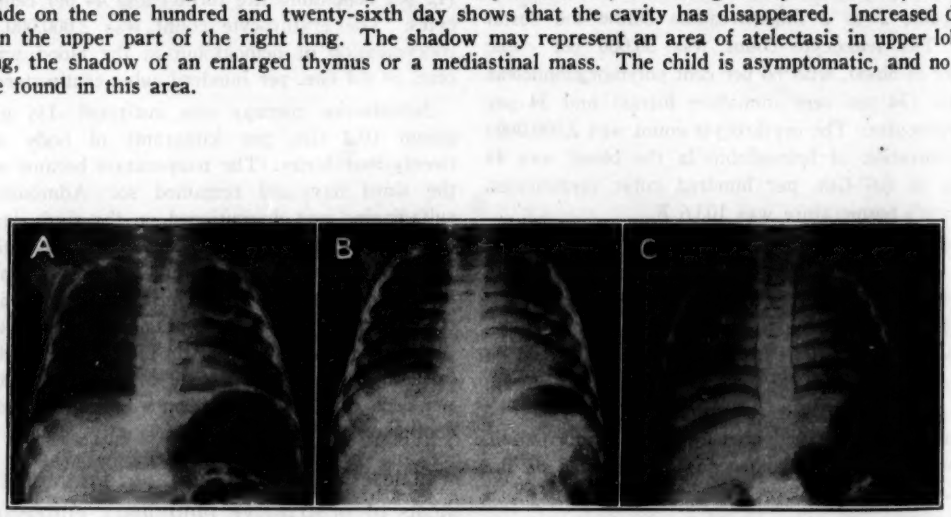

Fig. 2.—Chest of the patient in case 2. *A*, roentgenogram made on the day of admission shows an are decreased density, measuring 2 by 3 cm., in the upper lobe of the left lung, with a small amount of infiltra in the surrounding parenchyma. The cavity has a sharp, thin, dense margin. *B*, roentgenogram made on third day shows that the cavity is about the same size, but the margin of the cavity is not so well defined. roentgenogram made on the tenth day shows that the cavity is greatly reduced in size.

ns and the typical clinical course were present. a final result clear pulmonary fields were served in both cases.

COMMENT

The diagnosis of obstructive pulmonary physema is made on the characteristic roentnographic picture, the clinical course and the sence of physical signs. The roentgenographic pearance is typical, especially when the pulnary fields are clear. The emphysematous a consists of an abnormal region of decreased nsity, which is surrounded by a thin, dense smooth, margin. The area is usually ovoid, it is occasionally spheroid and sometimes ulated; it varies from very small to extremely ge, and it may occupy a large portion of the lmonary field. A characteristic feature is the riation in size of the lesion that occurs from ne to time. The duration of the lesion is ually a matter of weeks, but occasionally it y be months before the pulmonary fields beme normal. The cavity may contain fluid.

The clinical course after the pneumonic lesion s completely cleared is entirely asymptomatic. here is no elevation in the temperature or the lse rate; the leukocyte count is normal; there no clubbing of the fingers, no foul-smelling utum and no cough. The patient appears well d gains weight, and there are no abnormal ysical signs.

If signs and symptoms of an acute infection rsist, i. e., elevated temperature and leukocyte unt, a secondary complication, especially otitis edia, should be suspected.

No treatment is necessary unless a complicaon develops.

It has not been possible to make a direct rrelation between these lesions and the actual atomic changes in the lungs because the benign urse and the complete recovery of all patients ve not permitted the examination of the lungs, ther by surgical procedure or by necropsy.[2]

The differential diagnosis is easily made if e case is closely followed. During the actual fection, when the surrounding pulmonary lds are consolidated, the emphysematous area not clearly outlined, and its margins are distinct. Thus it may be impossible to rule out scess of the lung. Once the pneumonic process resolved, the characteristic roentgenographic cture makes itself evident, and the diagnosis comes clear. Congenital cysts of the lung in e early stages are usually solid fluid cysts. An ovoid opaque area is seen in the parenchyma of the lung, which persists unchanged in size over a long period. Later, when the fluid is replaced by air, the cyst wall is seen as a rather thin capsule. Not infrequently, fine strands or thin bands are seen traversing the structureless cystic space in wide sweeping curves. The roentgenoscope may reveal an increase in illumination within the cyst during inspiration.[3] Communication of the cyst with the bronchus can be shown by introducing iodized oil and outlining the lesion. This procedure will aid in differentiating a cyst from obstructive emphysema, for there is no direct communication between an emphysematous area and a bronchus. Kaltreider and Fray [4] expressed the opinion that pulmonary cysts are always in communication with the outside air, for if this were not true the air would soon be absorbed and the walls collapse.

In localized pneumothorax the air is seen outside the parenchyma of the lung, and occasionally fine bands are seen traversing the space in straight lines.

Diaphragmatic hernia can always be excluded by means of a meal of barium sulfate outlining the intestine.

Cavitation due to tuberculosis is excluded by negative reactions to cutaneous tests and by absence of tubercle bacilli in the sputum and in gastric washings.

The mechanism that produces the localized obstructive pulmonary emphysema is satisfactorily explained by a "check valve" type of obstruction, described by Jackson and Jackson.[5] Hoover [6] demonstrated, by means of animal experimentation, that when expiration was obstructed with a valve flap while free inspiration was allowed a lung became emphysematous. Van Allen [7] demonstrated that the expiratory, and not the inspiratory, obstruction of an entire lobe led to emphysema of that lobe; if smaller units were so treated, they did not become emphysematous, because of the collateral circulation

2. Caffey, J.: Regional Obstructive Pulmonary physema in Infants and in Children, Am. J. Dis. hild. **60**:586 (Sept.) 1940.

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4. Kaltreider, N. L., and Fray, W. W.: Pathological Physiology of Pulmonary Cysts and Emphysematous Bullae, Am. J. M. Sc. **197**:62, 1939.

5. Jackson, C., and Jackson, C. L., in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1932, vol. 4, chap. 7; in Brennemann, J.: Practice of Pediatrics, ibid., 1944, vol. 2, chap. 50, p. 2.

6. Hoover, C. F.: Tracheal and Bronchial Stenosis as Causes for Emphysema, Arch. Int. Med. **29**:143 (Feb.) 1922.

7. Van Allen, C. M.: Obstructive Pulmonary Emphysema and Collateral Respiration, Surg., Gynec. & Obst. **55**:303, 1932.

of air. Kountz and Alexander[8] expressed the view that there are spasm and actual hypertrophy of the muscle fibers of the 3 to 8 mm. bronchioles and that after inspiratory distention of the smaller lobules these air passages may become constricted and thus retain increased residual air. This opinion is compatible with Van Allen's conclusions only if all adjoining lobules are affected at the same time, as is probably the case; otherwise, because of the collateral respiration, the residual air would escape.

Thus it can be definitely stated that obstructive emphysema is a lobar phenomenon unless something is present to interfere with the collateral respiration.[9] The collateral circulation of air that exists in the lungs is due to combined action of the pores of Kohn and to direct diffusion of air through the alveolar septums. Ogawa[10] has shown by special histologic methods, by which the alveolar septums can be viewed in face as well as in cross section, that the pores actually exist. They are seen as oval openings in the surface, with smooth borders formed by the epithelial cells lining the alveoli. That air can pass from one lobule to another was shown by Van Allen, Lindskog and Richter.[11] If the bronchus of a division of a lobule in one pulmonary lobe of a living dog is obstructed, spontaneous and free inspiration and expiration may take place through another channel and the division maintain its inflation. Thus collateral circulation of air is prevented by existence of a complete septum between lobules and by inflammatory consolidation of the tissues at the border between the full and the obstructed portion of the lobe.[9]

During pneumonia conditions favorable for obstruction of the collateral circulation of air and to a "check valve" obstruction of one of the bronchi are present. The bronchus is blocked by a firm mass of exudate or viscid secretion, permitting the air to pass on inspiration but not to escape on expiration. The entrapped air causes an emphysematous reaction, and because of the presence of an inflammatory exudate in the alveolar spaces, the air is unable to escape. After resolution of the pneumonic process there is no possible route for the air to escape, since the margin of the emphysematous area is composed of compressed alveolar septums and the pores of Kohn are closed. Eventual resolution probably occurs by means of slow diffusion of air through the margin of the area or by removal of the initial obstruction. The length of time that the lesion takes to resolve probably depends on the manner in which the air escapes; if by diffusion it will clear slowly; if by removal of the obstruction it will clear rapidly. The final picture is one of complete restoration to normal, roentgenographically shown by pulmonary fields of the same density.

26 East Sixty-Third Street.

111 East Seventy-Seventh Street.

8. Kountz, W. B., and Alexander, H. L.: Emphysema, Medicine **13**:251, 1934.

9. Golden, R.: Abnormally Wide Respiratory Movement of Lower Lung Structures; Roentgen Evidence of Obstructive Emphysema, Am. J. Roentgenol. **44**:325, 1940.

10. Ogawa, O.: Contributions to the Histology of the Respiratory Spaces of Vertebrate Lungs, Am. J. Anat. **27**:333, 1920.

11. Van Allen, C. M.; Lindskog, G. E., and Richter, H. G.: Collateral Respiration: Transfer of Air Collaterally Between Pulmonary Lobules, J. Clin. Investigation **10**:559, 1931.

CHRONIC PYELONEPHRITIS WITH RENAL ACIDOSIS

M. G. PETERMAN, M.D.
MILWAUKEE

The present case of chronic pyelonephritis with al acidosis due to failure of the renal tubules reabsorb base carbonate is the first to come to attention. In December 1939 Hartmann[1] scribed the first case of primary renal acidosis th tubular insufficiency on record. His patient s a 4 month old infant with no history of al infection. There was, however, severe, un-mpensated renal acidosis with loss of base car-nate. Apparent complete recovery followed ministration of excessively large doses (75 cc. ily) of molar sodium r-lactate for several nths.

My patient was a 2 month old infant who was ought into the hospital with pyelonephritis and al acidosis. I was unable to clear the renal fection or to produce complete compensation the acidosis. After two months of intensive atment the patient died. The renal lesions are scribed in the present report.

REPORT OF A CASE

History.—Thomas C., a full term infant, was born g. 4, 1944, after a long (twenty-nine and one-half urs) and difficult delivery. He was an apparently nor-l, healthy boy, weighing 3,400 Gm. (7½ pounds). 3 days of age impetigo developed, which was treated th ammoniated mercury ointment for two weeks. The fant was said to have had heavy breathing from birth d to have choked on his feedings; he failed to gain yond his weight at birth and had much "gas on his mach." He was admitted to Milwaukee Children's ospital to my private service on Oct. 13, 1944.

Physical Examination and Laboratory Data.—The fant was poorly developed, poorly nourished and pale d had a feeble cry. He had air hunger, which varied severity throughout his illness. There were signs of small area of atelectasis in the upper lobe of the ht lung and a hydrocele of the right testis; the t testis was of pea size. The rectal temperature s 100.6 F., and it remained elevated throughout his y in the hospital. The blood count showed 11 Gm. hemoglobin per hundred cubic centimeters (Sanford-eard) and 3,120,000 erythrocytes and 23,000 leuko-tes per cubic millimeter, of which 42 per cent were utrophils, 50 per cent small lymphocytes, 1 per cent rge lymphocytes, 4 per cent mononuclear forms, 1 r cent eosinophils and 2 per cent plasma cells. The ine was strongly alkaline and showed a 1 plus re-tion for albumin, and 30 pus cells per high power ld, with clumps, and an occasional erythrocyte.

Treatment and Courses.—Eighty cubic centimeters of citrated whole blood was transfused on October 13 and the same amount on October 14.

October 15: Sulfacetimide in 0.5 Gm. doses was given twice, and thereafter 0.25 Gm. of the drug was administered three times a day. The respirations were still labored, and a third transfusion of 80 cc. of citrated whole blood was given.

October 16: The infant's color was much better than before, but his abdomen was distended, and the edge of the spleen was palpated. The blood count showed 11 Gm. of hemoglobin per hundred cubic millimeters and 4,290,000 erythrocytes and 11,000 leukocytes per cubic millimeter. The urine was strongly alkaline and showed a 1 plus reaction for albumin and 15 pus cells per high power field.

October 17: There was considerable air hunger, which could not be relieved with inhalation of oxygen. Two hundred cubic centimeters of lactate-Ringer (Hartmann's) solution was given subcutaneously and resulted in considerable improvement in breathing. The sulfacetimide was replaced with sulfadiazine, 0.5 Gm. being given again in one hour and then 0.25 Gm. every six hours.

October 18: The leukocyte count was 23,600 per cubic millimeter. Two hundred cubic centimeters of lactate-Ringer solution was given subcutaneously.

October 19: Air hunger was again prominent, and 200 cc. of lactate-Ringer solution was given subcutaneously. Administration of sulfadiazine was discontinued.

October 20: Air hunger was pronounced. The alkali reserve of the blood was 43 per cent; the nonprotein nitrogen measured 47.7 mg. and the sugar 83.5 mg. per hundred cubic centimeters.

The blood count showed 13.5 Gm. of hemoglobin per hundred cubic centimeters and 22,300 leukocytes per cubic millimeter. Two hundred cubic centimeters of lactate-Ringer solution was given subcutaneously, and 15 cc. of an alkaline solution (Liquid Citralka[2]) was given in two doses, with relief of the difficult breathing.

October 21: The breathing continued to be normal. The urine showed a 1 plus reaction for albumin and 10 pus cells per high power field, with clumps. Sulfacetimide was given, 0.5 Gm. every six hours. Liquid Citralka, 4 cc., was given every six hours.

October 22 and 23: The respiration was labored, and 200 cc. of lactate-Ringer solution was given subcutaneously. Administration of sulfacetimide was discontinued.

October 24: The infant had spells of air hunger, and the skin was ashen gray. The rectal temperature rose to 105 F. The alkali reserve of the blood was 10 per cent; the phosphorus measured 3.8 mg. per hundred cubic centimeters, the p_H was 6.4. The blood count showed 9 Gm. of hemoglobin and 3,540,000 erythrocytes and 25,000 leukocytes per cubic millimeter. The urine was still strongly alkaline and showed a trace of albumin

1. Hartmann, A. F.: Clinical Studies in Acidosis d Alkalosis, Ann. Int. Med. **13**:940 (Dec.) 1939.

2. Marketed by Parke, Davis and Company, Detroit. It contains 120 grains per fluid ounce (0.26 Gm. per cubic centimeter) of disodium hydrogen citrate.

and 6 white blood cells and an occasional red blood cell per high power field. One hundred cubic centimeters of lactate-Ringer solution was given subcutaneously. Ninety cubic centimeters of citrated whole blood and 200 cc. of 5 per cent dextrose in isotonic solution of three chlorides were given intravenously. Liquid Citralka, 4 cc., was given every four hours to November 2.

October 25: The rectal temperature rose to 105 F. The urine was strongly alkaline and showed a trace of albumin and 20 pus cells, with many clumps, and an occasional red blood cell per high power field. There were many renal epithelial cells. Ninety cubic centimeters of citrated whole blood and 200 cc. of 5 per cent dextrose in lactate-Ringer solution were given intravenously. The infant's color and breathing showed considerable improvement.

October 26: The clinical condition seemed better. The urine was acid and showed a trace of albumin and an occasional white blood cell. A transfusion of 90 cc. of citrated blood was given.

October 27: The rectal temperature ranged from 96.4 to 104.2 F. The alkali reserve of the blood was 32.4 per cent, and the nonprotein nitrogen measured 45 mg. per hundred cubic centimeters. The blood count showed 15.5 Gm. of hemoglobin per hundred cubic centimeters and 4,530,000 erythrocytes and 29,200 leukocytes per cubic millimeter. The urine was again alkaline and showed a 3 plus reaction for albumin, 60 leukocytes per high power field, with clumps, and 15 red blood cells per high power field. Administration of sulfathiazole was started, 1 Gm. in divided doses.

October 28: The air hunger increased. The urine was alkaline and showed 1 plus reactions for albumin and acetone and 10 white blood cells per high power field. A culture of the blood was sterile. The sulfathiazole was increased to 1.25 Gm., given in divided doses.

October 29: The rectal temperature ranged from 97 to 101 F., and the patient had profuse diaphoresis. Sulfathiazole was given, 1 Gm. in divided doses.

October 30: The blood count showed 14 Gm. of hemoglobin per hundred cubic centimeters and 5,290,000 erythrocytes and 14,200 leukocytes per cubic millimeter. The urine was alkaline, with a p_H of 7.5; there were a trace of albumin and 3 white blood cells per high power field. A culture showed Escherichia coli. Administration of sulfathiazole was continued, 1 Gm. being given in divided doses.

October 31: The patient had good color and tone and was gaining weight. The urine was alkaline but clear; the ratio of ammonia to titratable acid was 0.5. The sedimentation rate was 11 mm. in one hour (Westergren).

November 2: The urine continued to be persistently alkaline, with traces of albumin, and showed occasional clumps of pus cells. The blood count showed 12 Gm. of hemoglobin per hundred cubic centimeters and 4,750,000 erythrocytes and 16,000 leukocytes per cubic millimeter.

November 3: Administration of molar sodium lactate solution was started, 5 cc. being given every four hours. The sulfathiazole was replaced with sulfacetimide, 0.75 Gm. daily being given in divided doses up to November 12.

November 4: The Mantoux test (0.001 mg.) gave negative results.

November 7: A culture of the urine showed E. coli. The blood count showed 11.5 Gm. of hemoglobin per hundred cubic centimeters and 4,440,000 erythrocytes and 28,600 leukocytes per cubic millimeter. The patient had fever and increased air hunger. His weight remained stationary. Sixty cubic centimeters of lactate-Ringer solution was given subcutaneously every hours. The dose of molar sodium lactate solution increased to 7 cc. every four hours. The daily do of sulfacetimide were increased to 1 Gm., in divi doses.

November 8: The molar sodium lactate solution increased to 55 cc. daily, given in divided doses.

November 9: The urine continued to be alkaline showed pus cells. The alkali reserve was 52 per ce the level of sulfacetimide in the blood was 5.6 per hundred cubic centimeters, and the excretion phenolsulfonphthalein was 60 per cent in two hours.

November 11: The urine was still alkaline showed a 1 plus reaction for albumin and up to 30 cells per high power field. The sulfacetimide replaced with sulfanilamide, 1 Gm. being given da in divided doses, and the administration of molar sodi lactate solution was increased to 60 cc. per day.

November 13: The blood count showed 10.5 G of hemoglobin per hundred cubic centimeters 3,970,000 erythrocytes and 17,800 leukocytes per cu millimeter.

November 14: A culture of the urine yielded pathogens.

November 15: The blood count showed 11 Gm. hemoglobin per hundred cubic centimeters and 3,910,0 erythrocytes and 20,000 leukocytes per cubic millimet

November 16: Administration of sulfanilamide discontinued.

November 19: The air hunger increased, and rectal temperature rose to 104.8 F. The infant h spells of hard crying, as if in colic. (Was he passi crystals of calcium phosphate?)

November 20: One specimen of urine was acid showed a trace of albumin and 20 pus cells per h power field.

November 22: The urine showed crystals of calci phosphate, and a culture yielded E. coli and gra positive cocci. The Mantoux test (0.01 mg.) gave negative reaction. Sulfacetimide was given, 1 Gm., a later 0.25 Gm., every four hours.

November 24: The patient became weak and h increased air hunger. The blood count showed 1 Gm. of hemoglobin per hundred cubic centimeters a 4,180,000 erythrocytes and 13,200 leukocytes per cu millimeter, of which 62 per cent were polymorph nuclears, 34 per cent small lymphocytes, 1 per c basophils, 1 per cent monocytes and 1 per cent plas cells. The molar sodium lactate solution was increas to 72 cc. per day.

November 28: The Mantoux test (0.02 mg.) ga negative results.

November 30: Penicillin was given, 5,000 units be administered intramuscularly every two hours u December 5.

December 4: The p_H of the urine was as follow 12 noon, 6; 6 p. m., 7.5; 11 p. m., 7; 6 a. m., 6.5, a 10 a. m., 7.5.

December 5: The molar sodium lactate solution w increased to 90 cc. daily.

December 7: The blood count showed 10.5 Gm. hemoglobin per hundred cubic centimeters and 3,520,0 erythrocytes and 15,600 leukocytes per cubic millimet of which 48 per cent were polymorphonuclear form 37 per cent small lymphocytes, 1 per cent large lympho cytes, 5 per cent eosinophils, 1 per cent basophils, per cent monocytes and 1 per cent plasma cells. culture of the blood was sterile.

December 8 and 9: There was pronounced air hunger. The urine was packed with pus cells, and there were many renal epithelial cells with fatty degeneration. Red renal cells persisted to the end.

December 10 to 14: The child's color was better and the breathing normal. The urine contained 8 pus cells per high power field.

December 14: The air hunger increased. The alkali reserve of the blood was 17.5 per cent. The blood count showed 12 Gm. of hemoglobin per hundred cubic centimeters and 4,350,000 erythrocytes and 16,400 leukocytes per cubic millimeter; the sedimentation rate was 3 mm. in one hour.

December 18: The alkali reserve of the blood was 30 per cent. The blood count showed 12 Gm. of hemoglobin per hundred cubic centimeters and 5,100,000 erythrocytes and 26,800 leukocytes per cubic millimeter.

December 19: The rectal temperature rose to 106 F. and remained high to the end. The infant had recurring convulsions. The leukocyte count was 27,000; the level of nonprotein nitrogen in the blood was 36.3 mg. per hundred cubic centimeters, and a culture of the blood was sterile.

December 20: The spinal fluid was clear, colorless and under no increased pressure. It contained 1 cell per cubic millimeter, no globulin and 15 mg. of protein and 71 mg. of sugar per hundred cubic centimeters.

December 21: The blood sugar measured 74.5 mg. per hundred cubic centimeters.

December 22: The patient died.

Postmortem Examination.—A postmortem examination was made by Dr. G. H. Hansmann. The only significant abnormalities were found in the kidneys. The following description is taken from the report of autopsy:

"The kidneys were severely injured. A few glomeruli revealed thickening of the Bowman capsule and sclerosis, and a few others contained hyaline thrombi. The main trouble, however, appears to have been in the collecting tubule part of the kidneys, the damage increasing in severity as the tips of the pyramids were approached. In fact, many of the tips of the pyramids were ulcerated and had sloughed away. The reason for this seems to have been severe injury to the epithelium lining the tubules and the tissue immediately adjacent to them. Many tubules were filled with a granular precipitate; flattened masses of this material stained intensely blue with hematoxylin and were characteristic of the presence of calcium in the tissue. In fact, when the gritty material was tested for calcium urates and sulfonamide compounds, it burned with a distinct calcium flame, and it had a metallic tinkle when it was shaken in a glass tube. Tests for urates and sulfonamide compounds gave negative results. The calcium seemed to have incrusted and petrified epithelial cells, collagen bundles and cells making up the basement membrane. The material had no regular form. It appeared largely to conform to the structures impregnated. There was evidence of replacement with organized and fibrous tissue between these deposits of calcium. The child had periods of severe nephritic acidosis. The urine was found on only one occasion to turn acid to litmus paper.

"The mechanism in this instance seems to have been primarily injury to the epithelium, especially the epithelium lining the collecting system of the kidneys, although the cells of the convoluted tubules revealed some parenchymatous degeneration. The injury to the tissue increased in severity as the apex of the pyramids was approached. The injured tissue appears to have been subsequently impregnated and incrusted with calcium. I had not observed this condition prior to the administration of sulfonamide compounds. It is my opinion that the sulfonamide compounds injured the tissue, after which calcium impregnated it—the debris, dying cells or injured collagen. The injury paralleled the concentration of the injurious agent as it passed down the tubules. The tissue around the pelves was edematous and contained numerous inflammatory cells. There were occasional inflammatory cells between the masses of calcium, and the glomeruli contained more inflammatory cells than normal. I am of the opinion that these findings denote chemical irritation rather than infection."

COMMENT

The infant in the case reported here was admitted to the hospital with air hunger, fever, anemia, leukocytosis and pyelonephritis. The air hunger was due to uncompensated renal acidosis and had apparently been present from early life. It is possible that the pyelonephritis was congenital or appeared in the first days of life. This infection may have damaged the renal tubules sufficiently to have caused their inability to reabsorb the base carbonate. It is possible that application of ammoniated mercury to the skin for two weeks caused additional damage to the tubules. It is difficult to understand the failure to control the renal infection with sulfacetimide, sulfadiazine, sulfanilamide and sulfathiazole, since the urine was strongly alkaline. However, it is well known that the sulfonamide compounds are not effective in the presence of renal calculi. It might be assumed that the acidosis was secondary to the damage to the tubules. It is difficult to understand the apparent response to alkali therapy and the subsequent recurrences accompanying administration of extremely large doses (90 cc. per day) of molar sodium lactate solution. The large amount of amorphous calcium which filled the renal pelves was probably calcium phosphate. While it is possible, as the pathologist suggested, that the sulfonamide compounds damaged the renal tubules to some extent, it is much more plausible that the damage to the kidneys was present before the sulfonamide compounds were given. The clinical picture was present on the patient's admission to the hospital. No sulfonamide compounds had been given previously. It is recognized that phosphaturia may be accompanied with a renal disturbance which involves the acid-base regulation.[3] Von Reuss stated that

3. von Pfaundler, M., and Schlossmann, A.: The Diseases of Children, translated by M. G. Peterman, Philadelphia, J. B. Lippincott Company, 1935, vol. 5, p. 22.

precipitates are found with special frequency in the urinary tubules of newborn infants.[4] Holt stated that in over 1,000 postmortem examinations of infants small renal calculi were commonly found.[5] Calcium phosphate crystals were found in the present patient's urine early in the course of his disease, as were renal epithelial cells. The mortar-like masses of calcium in the renal tubu may have provided the source of constant irri tion which caused the continued recurrence pyelonephritis. There was no evidence of into cation with sulfonamide compounds. The cl ical course of the disease was characterized air hunger, fever, leukocytosis, anemia a pyuria. The renal acidosis was due to an compensated loss of bicarbonates. Treatm was wholly ineffective and death was apparen due to renal failure.

411 East Mason Street (2).

4. von Reuss, A. R.: Diseases of the Newborn, New York, William Wood & Co., 1921.

5. Holt, L. E.: Diseases of Infancy and Childhood, ed. 2, New York, D. Appleton and Company, 1902, p. 675.

Progress in Pediatrics

AMYOTONIA CONGENITA (OPPENHEIM)

REPORT OF FIVE CASES WITH NECROPSY; DISCUSSION OF THE RELATIONSHIP BETWEEN AMYOTONIA CONGENITA, WERDNIG-HOFFMANN DISEASE, NEONATAL POLIOMYELITIS AND MUSCULAR DYSTROPHY

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Amyotonia congenita (Oppenheim) is a rare sease. Since its differentiation by Oppenheim 1900 from the general group of wasting dises, there have appeared in the world's literare reports of about 200 cases, only about 50 which have included observations at necropsy. The clinical syndrome is reasonably definite, t the pathologic changes found at necropsy ve not been entirely uniform. Little is known out the etiology or pathogenesis of the disease. he cases reported here seem to shed new light the genetic nature of the disorder.

CLINICAL AND PATHOLOGIC PICTURE

The outstanding feature of amyotonia congen- is underdevelopment and hypotonicity of the eletal musculature. The disease is first appart in early infancy, and there is evidence [1] that antedates birth. The hypotonicity interferes ith normal postural development. When the sease is severe, the infant is never able to hold its head or to sit erect. When it is milder, ese acts are achieved at an age considerably ter than normal; in some cases even walking ith a peculiar waddling gait may ultimately come possible. Of 77 children over the age 16 months, walking was possible for 13.[2] For ose persons in whom the hypotonicity involves e intercostal muscles, pneumonia is a frequent rminal complication before the end of the first ar of life. In those in whom the muscles concerned with respiration are spared, the disease is apt to run a longer course, sometimes marked with periods of apparent improvement, but most children afflicted with amyotonia congenita succumb to intercurrent infection before adult life is reached.

Complete recovery has never been reported, although there are occasional reports of cases in which the disease has remained stationary for years.[3]

The condition of the musculature, as reported, has been found fairly uniform.[4] Clinically, the muscles are weak but not paralyzed. They show quantitative reduction or absence of electrical responses; they do not show the reaction of degeneration. Tendon reflexes are weak or absent. At necropsy the muscles are observed to be small and pale, and sometimes they are thin enough to be described as translucent. Microscopically, the picture is that of embryonic muscle; most fibers are small, and some are of normal size. There is a decided increase in sarcolemma nuclei. Both fat and connective tissue within the muscles are increased, but there is practically universal agreement concerning the absence of signs of degeneration with the muscles.

The pathologic changes found in the nervous system have not been as consistent as those in the musculature. In some cases [5] no abnormality

From the Children's Hospital and the Laboratory of eurology, George Washington University.

1. (*a*) Turner, J. W. A.: The Relationship Between myotonia Congenita and Congenital Myopathy, Brain :163, 1940. (*b*) Foot, N. C.: Report of a Case of myotonia Congenita (Myatonia Congenita-Oppenim) with Autopsy, Am. J. Dis. Child. **5**:359 (May) 13. (*c*) Faber, H. K.: Amyotonia Congenita: A rvey of the Known Cases with a Report of Three ew Cases, ibid. **13**:305 (April) 1917.

2. Reuben, M. S.: Amyotonia Congenita of Oppenim: A Report of Six Cases with a Full Review of e Literature, Arch. Int. Med. **20**:657 (Nov.) 1917.

3. Benjamin, E. L.: Amyotonia Congenita: Report of Two Cases in the Same Family, Arch. Pediat. **48**:734, 1931.

4. (*a*) Grinker, R. R.: The Pathology of Amyotonia Congenita: A Discussion of Its Relation to Infantile Progressive Muscular Atrophy, Arch. Neurol. & Psychiat. **18**:982 (Dec.) 1927. (*b*) Conel, J. L.: Distribution of Affected Nerve Cells in a Case of Amyotonia Congenita, ibid. **40**:337 (Aug.) 1938; Second Case, Arch. Path. **30**:153 (July) 1940. (*c*) Reuben.[2] (*d*) Faber.[1c]

5. (*a*) Spiller, W. G.: The Relation of the Myopathies, Brain **36**:75, 1914. (*b*) Councilman, W. T., and Dunn, C. H.: Myatonia congenita: A Report of

(*Footnote continued on next page*)

in the spinal cord has been detected, but in the majority [6] a reduction in the number of cells in the anterior horns has been an outstanding observation. Most workers have reported deficient myelination of the peripheral nerve fibers and of the anterior roots of the spinal cord.[6a] The two points on which there is relative agreement among those workers who have found a disorder in the nervous system is, first, its location within the lower motor neuron [4b] and, second, the absence of secondary degeneration.[6a]

Other parts of the body have been found abnormal, particularly the various endocrine glands. The thymus,[7] the thyroid [5b] and the adrenals [8] have been considered factors in causing the syndrome of amyotonia. Manifold congenital malformations [9] have been observed in various cases of amyotonia and have led Lewey [9a] to postulate that the whole picture may be explained on the basis of a developmental retardation and malformation.

REPORT OF CASES

CASE 1.—M. T., a white girl, was 5½ months old when first seen. She was brought into our office with the complaint that "the baby has no use of herself." The mother was an adopted child and no information was available concerning her family. She herself was well. M. T. was the result of the mother's second pregnancy, M. E. T. (reported on in case 2) being the first child. She had had but two pregnancies. Both babies moved in utero but never vigorously. The father, one of fourteen children, was living and well. There was no history of any muscular difficulty in himself nor in any of his relatives.

The patient was born spontaneously at full term after a normal pregnancy and a normal labor. Her birth weight was 2,290 Gm. She was breast fed for two weeks and then given an evaporated milk formula supplemented with percomorph liver oil. No orange juice had been given. The baby never sucked vigorously, and she gained weight slowly. From birth, according to the mother, she did not use her arms and legs as other babies do. Her cry was always weak. She could never hold up her head and never made any effort to sit up or to crawl.

Physical Examination.—The infant was a 5½ month old white girl, with a weight of 6,000 Gm., a length of 65 cm. and a head circumference of 43 cm. She w poorly nourished and pale, and she lay quietly on t examining table. Her arms and legs moved very lit although she was able to move them away from pain stimuli. When she cried, the frontalis and the risori muscles contracted fairly well, and a weak cry like whisper was heard. She was unable to cough. S could not hold her head up when her back was su ported, nor could she turn her head to either si She could not sit up at all (fig. 1 *A*). She made effort to crawl or to turn over. Sucking was fai vigorous, but she became exhausted quickly. Breathi was entirely diaphragmatic; the intercostal muscles we thin and flabby and took no part in the respirato activity. With each inspiration the ribs flared out, t thorax was depressed and the abdomen increased size (fig. 1 *B*). The baby smiled at her mother a responded both to her mother's voice and to her fa Her eyes followed a light, and she fingered a toy wh it was placed within her reach.

Complete physical examination revealed no viscer disease. The arms and legs were thin and flabby.

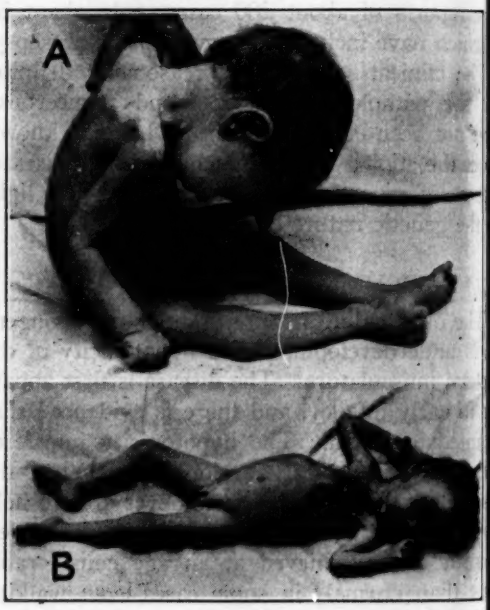

Fig. 1 (case 1).—*A*, patient doubled over, unable hold up the head; *B*, atonic limbs and thorax retract during inspiration.

tendon reflexes could be obtained and abdominal reflex were absent.

The baby was sent to the Children's Hospital, Was ington, D. C., on April 28, 1943 for a comple examination. She remained there for two weeks, duri which time the following laboratory data were recorde

The Kahn and the Mazzini flocculation tests of t blood elicited negative reactions. Determinations blood chemistry showed the sugar, nonprotein nitroge calcium and phosphorus levels to be within norm limits; the creatinine level was 0.7 mg. per hundr cubic centimeters (normal 1 to 3 mg.). The amyla activity of the blood was 16.7 units (normal).

A roentgenogram of the skull gave no evidence intracranial pressure; the sella turcica was normal.

Routine urinalysis, blood count and spinal fluid e amination revealed nothing of significance. Determin tions of the electrical reaction of muscles show chronaxia values over the seventh nerve of approx mately normal range (0.2 to 0.4 millisecond). Chronax

a Case with Autopsy, Am. J. Dis. Child. **2**:340 (Nov.) 1911. (*c*) Menges, O.: Ein Beitrag zur Pathologie der Myatonia congenita, Deutsche Ztschr. f. Nervenh. **121**:240, 1931.

6. (*a*) Holmes, J. B.: Amyotonia Congenita (Oppenheim): Report of a Case with Full Histopathologic Examination, Am. J. Dis. Child. **20**:405 (Nov.) 1920. (*b*) Grinker.[4a] (*c*) Reuben.[2]

7. Smith, A. J.: Histological Changes Encountered in the Thymus and Elsewhere in a Case of Congenital Hypotonia, Univ. Pennsylvania M. Bull. **18**:206, 1905.

8. Griffith, J. P. C., and Spiller, W. G.: Amyotonia Congenita—A Clinical and Pathological Study, Am. J. M. Sc. **142**:165, 1911.

9. (*a*) Lewey, F. H.: Myatonia Congenita (Oppenheim) Accompanied by Congenital Intraspinal Tumor, Developmental Retardation and Malformation, Am. J. Dis. Child. **63**:76 (Jan.) 1942. (*b*) Conel.[4b]

lues up to 4 milliseconds failed to elicit contractions er the following points: (*a*) ulnar and radial nerve unks on each side of the biceps, (*b*) motor points of the ceps, (*c*) motor points of muscles flexing the fingers, *d*) motor points of vastus internus and externus, (*e*) otor points of foot extensors.

Treatment and Course.—The baby was given a high itamin, high protein diet, and for a brief time she ined weight. Large doses of vitamin E (2 cc. of wheat rm oil daily), according to a recent suggestion,[10] ere given for several weeks without appreciable effect. After the study had been completed, the baby was sent me on Sept. 12, 1943. It was felt at this time that e prognosis was hopeless because of the extensive involvement of the thoracic musculature.

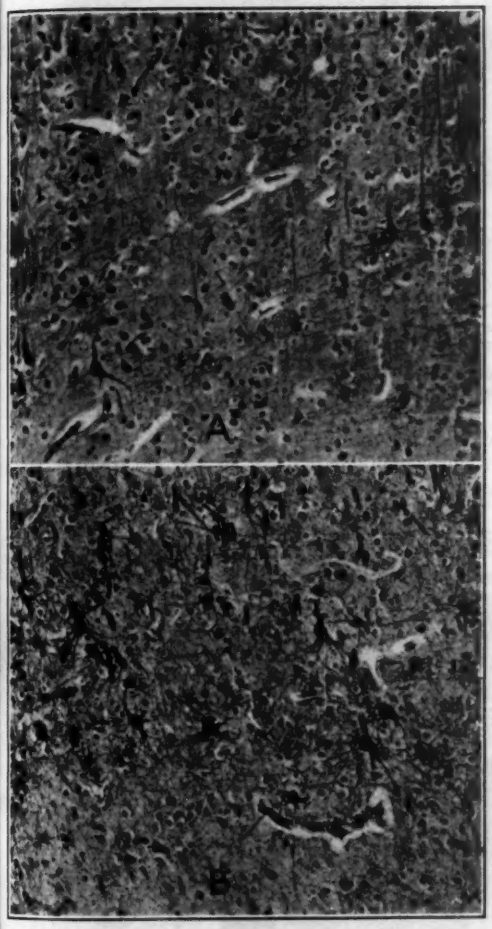

Fig. 2 (case 1).—*A*, precentral cortex, area 4, showg maximum collection of large motor cells. Bodian lver impregnation; × 120; *B*, normal control; × 92. rmy Medical Museum negative 83023.

The baby remained at home for one month, during hich time she was seen from time to time, and no sigficant change in her condition was noted.

When she was 8 months old, she was observed to ave a high fever and was readmitted to the hospital Oct. 14) with acute bronchopneumonia. In spite of lfadiazine and oxygen therapy she died two weeks ter, on October 28.

10. Stone, S.: Vitamin E in the Treatment of Muscle isorders of Infancy and Childhood, J. Pediat. **18**:310, 941.

Necropsy was performed four hours after death. The body was that of a poorly developed and poorly nourished baby girl measuring 66 cm. in length and weighing 5,160 Gm. There was no rigor mortis. The thorax was prominently increased in its anteroposterior diameter. The skin and subcutaneous tissues were flabby. The muscles showed striking pallor and translucency and were extremely small. The intercostal muscles were scarcely more than pinkish membranes; the diaphragm, on the other hand, was of normal thickness, color and consistency. Both lungs showed confluent bronchopneumonia; the other internal organs, including the endocrine glands, were approximately normal. The brain showed some venous congestion; the spinal cord was of average caliber. The anterior roots were extremely thin and translucent in comparison with the posterior roots.

Microscopic Examination.—A section of the paracentral lobule of the brain (the motor cortex) showed almost complete absence of the large multipolar Betz cells (fig. 2 *A*); otherwise, the cortical architecture of this and other areas was normal, and the ganglion cells showed only minor changes. Aside from congestion, meninges and brain tissue showed no signs of inflammation, atrophy or gliosis. The basal ganglions, midbrain and cerebellar structures were normal.

The motor nuclei from the facial to the hypoglossal nerve showed in varying degree a reduction in the number of large cells but no signs of inflammation or degeneration. The proportion of small multipolar cells was increased in these nuclei. The nucleus of the facial nerve was more severely affected than the others, but in none of them was the reduction comparable to the condition observed in the spinal cord.

The spinal cord revealed extreme paucity of anterior horn cells (fig. 3 *A*). At the same time there were no indications of degeneration as judged by cell stains and stains for fat, and none of the cells showed axonal reaction. Small ganglion cells were numerous in the anterior horn, and occasionally some irregular hyperchromatic cells were observed. The fibrillar architecture of the anterior horns was also noticeably reduced, and the anterior roots were small and almost entirely free of myelin. In contrast to the severe deficiency in the anterior horns, the lateral horns contained a normal number of elongated "sympathetic" cells, and the large cells in Clarke's column were strikingly preserved.

The myelin picture of the spinal cord was relatively normal, although the pyramidal tracts were composed only of small fibers with thin sheaths, contrasting rather strongly with the normal-appearing posterior columns. No abnormality was noted in the meninges or blood vessels. The spinal ganglions were normal; the cauda equina showed great contrasts between the healthy afferent roots and the tenuous efferent roots. The celiac ganglion was normal.

Several specimens of skeletal musculature were examined, and all showed much the same characteristics. A few large normal fibers with well marked longitudinal and crossed striations in small groups were scattered among a large number of small fibers with many perimysial nuclei (fig. 4). In certain muscles the proportion of large fibers was greater, and the small muscle fibers of fetal type were scattered in groups; there were few fibers of intermediate size. Nerve filaments could be found here and there, but nerve endings were present only on the large fibers, and they were few and simple. Muscle spindles were occasionally encountered. In contrast to the picture of the skeletal musculature, the heart, diaphragm and tongue showed no significant alterations from normal. There were no hypertrophied or obviously degenerated muscle fibers in any of the sections, and, although some

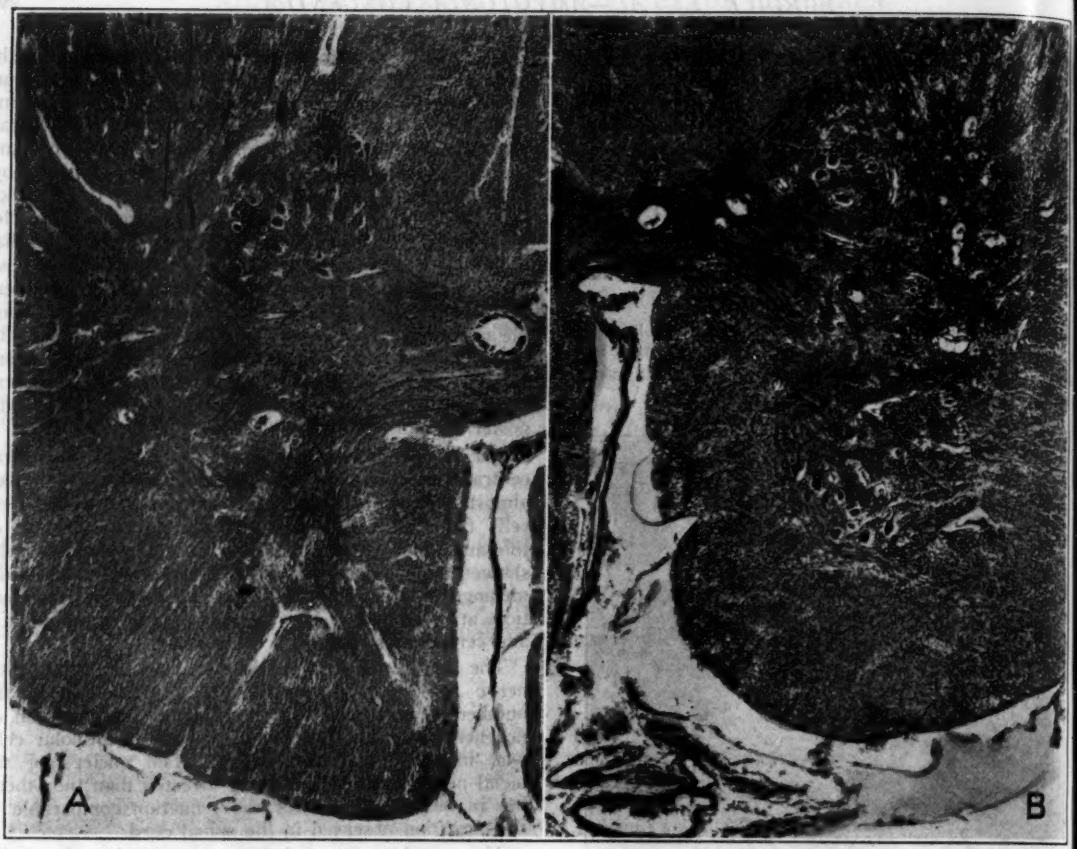

Fig. 3 (case 1).—*A*, thoracic portion of the spinal cord, showing paucity of anterior horn cells and rootle but preservation of cells in lateral and dorsal horns. Bodian silver impregnation; × 50. Army Medical Museu negative 77137; *B*, normal control; × 50; Army Medical Museum negative 83030.

Fig. 4 (case 1).—Vastus internus muscle, showing a few normally developed fibers in groups among nume ous small immature fibers; × 130; Army Medical Museum negative 77123.

uscle fibers contained more fine fat globules than hers, this was considered an indication of metabolic tivity rather than degeneration, since the sarcoplasm d nuclei appeared normal. There was an apparent, t probably only relative, increase in the perimysial nnective tissue. Smooth musculature from the pylorus, adder, uterus and major arteries revealed no defects.

CASE 2.—M. E. T. was the first child born to the other of M. T. (case 1). The patient was not seen any of us, but information obtained from the mother, om the hospital record of the baby's terminal illness d from a reexamination of the microscopic sections tained a necropsy seem to us sufficient to justify a obable diagnosis of amyotonia congenita.

M. E. T. was born spontaneously at full term and eighed 2,900 Gm. She was apparently normal at rth, although the mother reported that she always emed weak. She sucked vigorously for a few minutes t was fatigued quickly. She never held up her head or oved her arms and legs as other babies do. The y was always weak. In spite of the difficulties, no edical care was sought until the child was 5½ months d, at which time she was brought to the hospital utely ill with bronchopneumonia. She died a few ours after admission. This child, seen only a few ours before death, was not given a thorough clinical amination, but it was observed that a thoracic deormity existed and that the intercostal muscles were nderdeveloped.

Necropsy was performed six hours after death. The ody was that of a poorly nourished white girl. There as no rigor mortis. The anteroposterior diameter of e chest was greater than the transverse diameter. The tercostal muscles were translucent. Unfortunately, her skeletal muscles were not examined, and the cord as not removed. Both lungs showed confluent bronchoneumonia.

Microscopic Examination.—The viscera showed varyg degrees of cloudy swelling of the parenchyma. ections of the frontal lobe, thalamus and midbrain ere normal.

CASE 3.[11]—L. C., a white boy, was 7 months old hen first seen. He was brought into the Children's ospital on May 19, 1944 because half an hour before dmission he had choked on a bit of cereal. The child ad first become blue and then an ashy gray color. he mother tried to relieve him by putting her finger own his throat; finally she gave him artificial respiraon, to which he eventually responded.

The mother was a healthy woman, aged 33 at the me of the birth of the patient. The father, aged 39, as also living and well. The family trees were traced ack on both sides for several generations, and no cases any disease even remotely resembling amyotonia were scovered. There were numerous cases of asthma in e family. There were two older children of these arents, a girl aged 9 and a boy aged 6 years. Both ere living and, except for frequent attacks of asthma the girl, were well.

The patient was born spontaneously at term after a ormal pregnancy. The mother stated that fetal movements seemed even more vigorous than with her previous children. She recalled having jokingly commented her obstetrician, "He must be going to be a football layer, he kicks so hard." No deformities were noted the infant at birth; he sucked the breast fairly well. e was breast fed for about two months and then was iven an evaporated milk formula, the usual accessory oods being fed in adequate amounts. There was a ndency for him to regurgitate liquids through his ose. The gain in weight was satisfactory until the age of 7 months, at which time the weight curve flattened a little.

The mother commented that the baby had seemed weak from birth. He did not move his arms and legs as much as her other babies. His cry was soft and weak, and his cough was weak and inadequate for clearing his throat. He never held up his head. He never made any attempt to sit up or to roll over. He objected to lying on his abdomen. He smiled at his mother and fingered a toy put into his hand but would make no effort to retrieve a lost toy. The mother stated that his muscular development had never started.

Physical Examination.—The boy was poorly nourished and pale but not acutely ill. He lay flaccid with head turned to the left and the left thigh drawn up medially. He fretted with a low-pitched whining cry; his mouth drooped at the corners. When the examiner made an attempt to pick him up by putting his hands under his armpits, no resistance was encountered and the baby "slipped through his hands." Breathing was entirely diaphragmatic. At times it was labored, and then the baby became somewhat cyanotic. The left side of the chest was more collapsed than the right side, and the anteroposterior diameter of the chest was greater than the transverse. The lungs and heart were normal as far as could be judged by physical examination. The abdomen and genitalia were normal. The muscles of the extremities were soft and flabby. There was a prominent pad of fat over the dorsum of each foot. The digits were longer than normal. Both deep and superficial reflexes were absent.

Fig. 5 (case 3).—Paracentral lobule, showing a few large pyramidal elements but no Betz cells. Compare figure 2*B* for control. Bodian silver impregnation. × 115.

The baby was admitted to the hospital for complete study, but after twenty-four hours his temperature began to rise and it was discovered that he had bronchopneumonia. Routine examination of the blood and urine revealed nothing significant. The baby was placed in an oxygen tent and given sulfadiazine and nikethamide, but he died on May 21, two days after admission. There had been no opportunity for further laboratory investigation. A partial autopsy was performed twenty-one hours after death. The brain, spinal cord and a portion of thigh muscle and of diaphragm were removed for sections.

The body was that of a poorly developed and poorly nourished white boy. The anteroposterior diameter of

11. Permission to report this case was granted by Dr. Hugh J. Davis.

the chest was greater than the transverse. Skeletal muscles were small and pale. The brain was normal; the spinal cord had extremely tenuous anterior roots but was itself of normal size and color. The rest of the organs were not remarkable. Microscopic examination revealed entire absence of the large multipol cells of Betz in the paracentral lobule although a fa number of large pyramidal cells were in eviden (fig. 5). Lamination and polarity were otherwise no mal. The gray masses elsewhere showed no significa

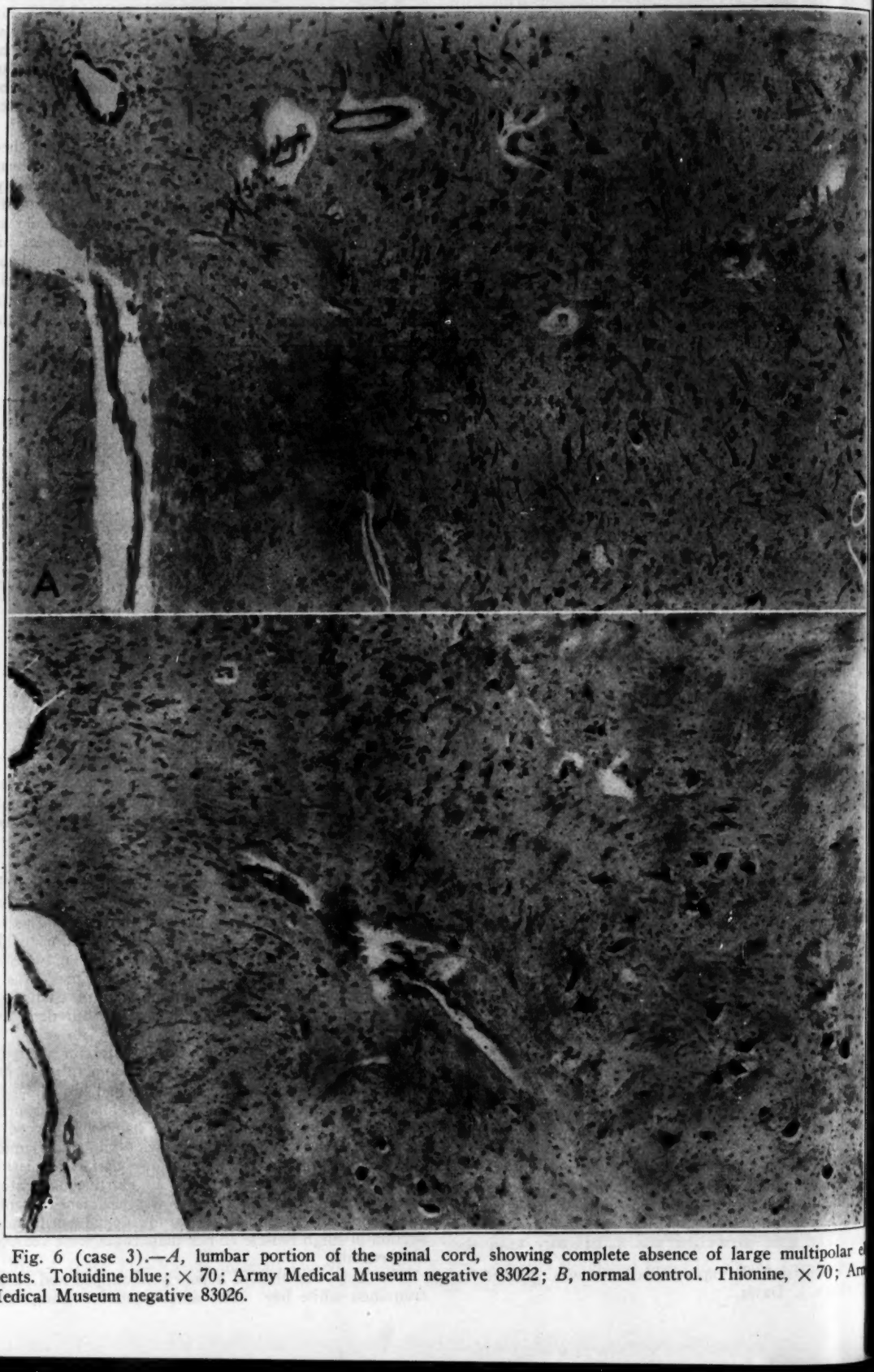

Fig. 6 (case 3).—*A*, lumbar portion of the spinal cord, showing complete absence of large multipolar c ments. Toluidine blue; × 70; Army Medical Museum negative 83022; *B*, normal control. Thionine, × 70; Arm Medical Museum negative 83026.

terations. In the brain stem the motor nuclei of the cranial nerves were approximately normal. On the other hand, the spinal cord showed striking to complete absence of the large multipolar cells in the anterior horns (fig. 6). The lateral and dorsal horns were well developed. Furthermore, the contrast between the anterior and the posterior roots was pronounced, the former containing only a small number of fibers. There were no indications of degeneration in either the ventral horns or the roots or in the long pathways of the spinal cord. The muscles revealed embryonal characteristics with occasional admixture of fibers of normal size. Here also there was no sign of degeneration. There were no end plates demonstrated on either normal or abnormal muscle fibers, although cross striations were clearly visible.

Case 4.[12]—D. H. was a white boy 11 weeks old. When first seen he was acutely ill with bronchopneumonia.

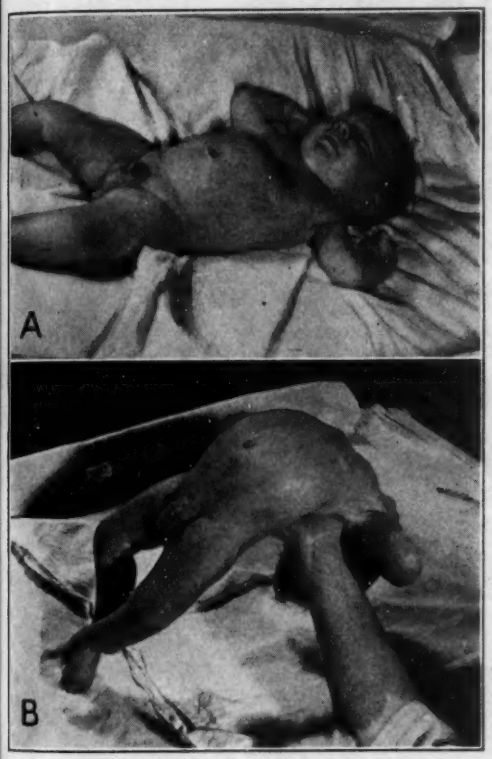

Fig. 7 (case 4).—*A*, child lying flaccidly in crib, showing retraction of thorax during inspiration; *B*, lack of tone in all the muscles when supported by the back.

Both the mother and the father were living and well. The mother was 27 and the father 39 at the time of this child's birth. There was one previous pregnancy, which resulted in a full term child who died during the neonatal period (case 5). Concerning fetal movements, the mother said that her first child moved much less in utero than her second. Whether this observation is significant of difference in muscular development between the 2 infants, it is impossible to say. The patient was born spontaneously at term after a normal pregnancy. The birth weight was 3,800 Gm. There was no evidence of birth injury.

12. Permission to report this case was granted by Dr. John H. McLeod.

The baby was fed an evaporated milk mixture from birth. He was given adequate supplements of cod liver oil and orange juice. He never sucked vigorously and was described as a slow eater. He gained weight slowly, weighing 4,800 Gm. at 11 weeks of age. He never held up his head and never made any attempt to roll over. He moved his arms and legs but little.

Physical Examination.—Measurement showed a head circumference of 40.7 cm. and a chest circumference of 35.5 cm. The boy was poorly nourished and acutely ill. He had much difficulty in breathing, with intercostal depression at each inspiration (fig. 7 *A*). Breathing was entirely diaphragmatic. The arms were kept flexed; the third, fourth and fifth digits on each hand were flexed and spastic. The legs were flaccid. There was little movement in either arms or legs. When the child was supported by the back, the head and legs almost met (fig. 7 *B*). Neither deep nor superficial reflexes could be elicited. The child's cry was a weak, whimpering sound. The frontalis and risorius muscles contracted weakly when the baby cried.

The mucous membranes were pale but otherwise normal. The ear drums were normal. The throat was somewhat injected; there were no teeth. There was no glandular enlargement. There was bronchopneumonia of the apex of the right lung extending to the fourth interspace. The heart was normal. The abdomen was soft. The genitalia were normal.

The baby was admitted to Children's Hospital on April 25, 1944, and the following laboratory data were obtained:

The Mazzini flocculation test of the blood elicited a negative reaction. Determinations of blood chemistry showed: creatinine, 0.5 mg. per hundred cubic centimeters (normal, 1 to 3 mg.), and creatine, 4.1 mg. (normal, 4 to 5 mg.). A twenty-four hour specimen of urine contained 2.2 mg. of creatinine nitrogen per kilogram of body weight (normal).

A roentgenogram of the skull showed a slight bulge in the soft tissue above the anterior fontanel. The cortex was somewhat thinner than normal. There was no evidence of fracture or of intracranial pressure. The sella turcica was normal. A roentgenogram of the long bones showed no abnormalities in the upper or lower extremities. A routine urinalysis, blood count and examination of the spinal fluid revealed nothing of significance.

The baby was put into an oxygen tent and given sulfadiazine by mouth. He improved; the pneumonia cleared to a considerable extent, although not completely. The child was discharged from the hospital on May 22 but was readmitted on May 26 because of difficulty in breathing, such as had occurred before. Bronchopneumonia developed, and he died on June 10. An autopsy was performed eleven hours after death.

The body was that of a poorly developed and poorly nourished white boy weighing 4,800 Gm. and measuring 62 cm. in length. There was a noticeable depression of the sternum and a slight flaring of the costal margin. The anterior fontanel was open and approximately 5 cc. of clear cisternal fluid was obtained. The intercostal muscles were thin and pale, as were all the other skeletal muscles. The diaphragm was normal in appearance, being possibly slightly thicker than that usually seen in a child of this age. The heart was normal, as were the rest of the viscera. Both upper and lower lobes of the right lung were completely consolidated. The left lung was pink and was crepitant throughout. Grossly the brain and spinal cord appeared normal.

Microscopic Examination.—In the brain the only departure from normal was an almost complete absence of the large multipolar Betz cells in the paracentral convolution (fig. 8). The cells present were smaller than normal. There were fairly numerous large pyramidal cells in this and the adjacent premotor areas, while the architecture of the postrolandic convolutions was entirely normal. There was no sign of inflammation or degeneration. The gray masses of the basal ganglions, cerebellum and brain stem were normal. The motor nucleus of the trigeminal nerve showed a moderate deficiency of cells, with no acute changes or reaction on the part of the glia.

The anterior horns of the spinal cord were almost devoid of large multipolar elements. Those remaining were sometimes rounded, with blunt heavy-staining processes, sometimes elongated, shrunken and overstained (fig. 9). There were a few locations in which it appeared that cells might have dropped out, but there was no reactive gliosis or inflammatory reaction. The cells of the lateral and posterior horns and of Clarke's column were well preserved by comparison. Fiber stains revealed paucity of intertwining fibers in the anterior horns and decided reduction in the size of the anterior roots, with an almost complete absence of heavy fibers. The peripheral nerves showed no indications of degeneration. It appeared that some of the fascicles were deficient in fibers and their sheaths, and there was some increase in the density of the perineurium.

Specimens of muscle were obtained both during biop and during necropsy. Special stains of the former r vealed a few simple nerve endings on cross-stria muscle fibers of normal size (fig. 10). No nerve e ings could be found in connection with the small mus fibers, which were in the majority. Muscle spind were normal. Further examination of the muscles r vealed that small groups of muscle fibers ranging to 50 microns in diameter were scattered here and th among small fibers. Dustlike particles that took t fat stain were present in the larger fibers but not the small ones. An occasional oversized fiber w paling of the striations seemed to indicate degenerati but such fibers were exceptional. There appeared be no excessive amount of fibrous tissue in connecti with the muscles.

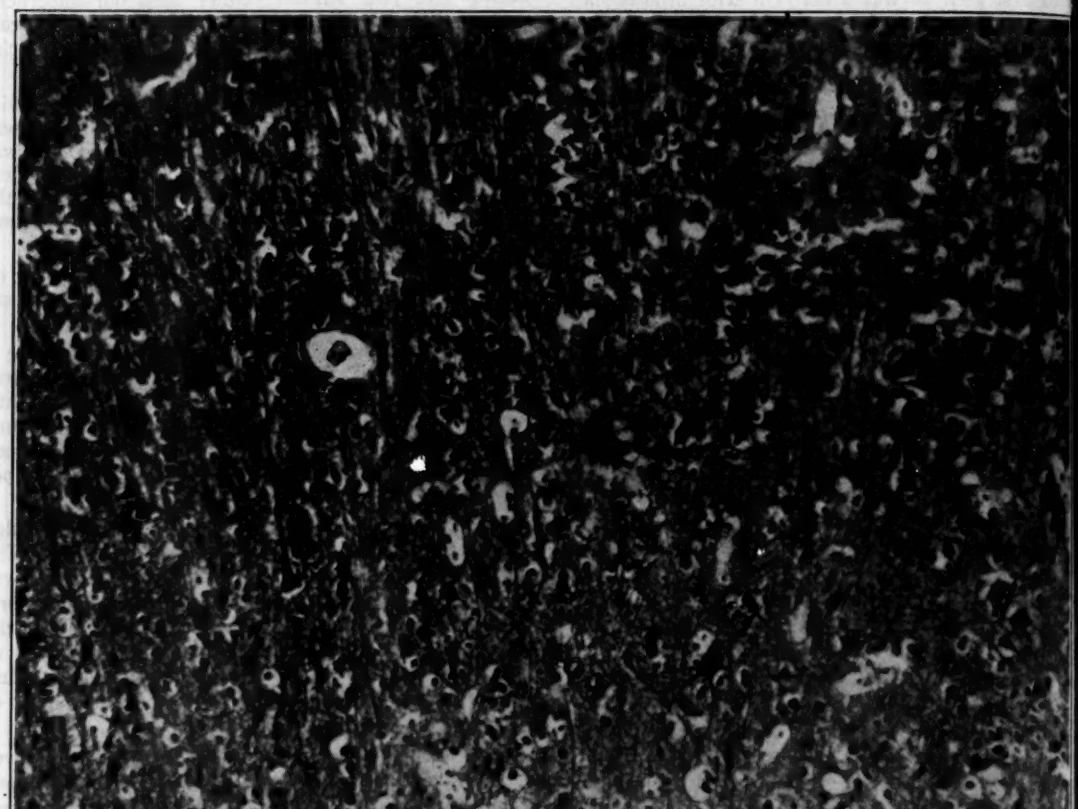

Fig. 8 (case 4).—Precentral cortex, area 4, showing maximum accumulation of large motor cells. Bodi silver impregnation; × 140. Compare with figure 2*B* for control.

CASE 5.[13]—W. H. was a white boy 6 weeks of a This patient was the first child born to the parents D. H. (case 4). He was brought into Children's Ho pital because of noisy grunting respiration. The moth had a full term normal pregnancy and fourteen hou of labor. The child weighed 3,500 Gm. at birth. The was no sign of intracranial injury at the time of d livery, and the child cried immediately after birt Paralysis of the right arm and hand was noted t second day after birth, but it diminished within a we or two. The baby was breast fed for two and a ha weeks and then given an evaporated milk mixture.

13. Permission to report this case was granted b Dr. Dorothy S. Jaeger.

He was admitted to Children's Hospital on Nov. 6, l. For the preceding two weeks the mother had ed grunting respiration when the baby was asleep. spiration had been more labored for the last few s. There had been no cough, although the baby ezed occasionally. No fever had been noted, and he k his feedings fairly well.

Physical Examination.—The patient was a thin henic type of baby, lying quietly on the table with

Fig. 9 (case 4).—Thoracic portion of the spinal d, showing paucity of cells in the anterior horn. lian silver impregnation; × 58.

y little movement of the extremities. The right arm wed flaccid paralysis. Breathing was accompanied h a grunting sound and was entirely diaphragmatic. e baby was dyspneic and slightly cyanotic.

A roentgenogram of the chest confirmed the clinical gnosis of bronchopneumonia. The baby was put into respirator, and the cyanosis disappeared. It was refore considered that the cyanosis was due to in- ivity of the intercostal muscles rather than to monary disease. Roentgenograms of the skull and g bones showed no abnormality. The Kahn reaction the blood was negative. Routine examination of od, urine and spinal fluid revealed nothing of sig- icance.

The course in the hospital was steadily downhill and baby died on Nov. 14, eight days after admission, the age of 6½ weeks.

Autopsy.—The body was that of a well nourished ite boy with a long narrow thorax. The weight was 51 Gm. and the length 58 cm. The intercostal scles were thin and translucent. The thymus was derately enlarged, weighing 12.5 Gm. The lungs owed bilateral atelectasis and fibrosis of the upper e of the right lung. The liver showed fatty infil- tion, and the spleen was enlarged. The brain was ssly normal.

Microscopic Examination.—In the two sections of brain available, the cortical architecture was entirely normal, with no hint of degeneration or gliosis. The precentral area was not available for study. The caudate nucleus and the cerebellum showed no changes.

The spinal cord was deficient in the large multipolar cells of the anterior horn (fig. 11). Those present were more or less normal in configuration but rather deep staining, with short blunt processes. Small triangular cells with rather large nuclei were often seen, suggesting immature elements. No oversized cells were seen, nor were any cells found in stages of acute chromatolysis. In contrast to the cells of the anterior horns, those of the lateral horns and of Clarke's column were remarkably preserved, and the small cells in the posterior horns were normal. While the anterior horns were substantially of normal size, they were deficient in the interweaving fibers that normally characterize this structure, and the intramedullary rootlets were strikingly absent. There was no indication of degeneration or reaction in the form of gliosis or infiltration. No definite indication of empty cell beds was observed, and there were no alterations in the capillaries, except for numerous ring hemorrhages in the central gray matter. The anterior roots were thin, with few axons and fewer myelin sheaths. These and the peripheral nerves showed no signs of trauma or degeneration.

EPITOME OF THESE CASES

1. Familial incidence; two families with 2 cases each.
2. Onset by the time of birth.
3. Hypotonicity of all skeletal musculature, including the intercostal muscles; muscles innervated by the cranial nerves were less severely affected than those innervated by spinal nerves.
4. Absence of tendon reflexes.
5. Absence of electrical excitability of muscles in the only case in which it was tested.
6. Low blood creatinine content in 2 cases tested.
7. Lack of involvement of involuntary musculature and diaphragm.
8. No clinical improvement.
9. Death from bronchopneumonia in infancy.
10. Embryonic type of skeletal musculature.

Fig. 10 (case 4).—Branching nerve fiber in connection with muscle fibers of normal size; no nerve endings seen. Silver impregnation; × 260.

11. Absence of degeneration in skeletal musculature.
12. Absence of large multipolar Betz cells in the motor cortex.
13. Paucity of anterior horn cells.
14. Decreased myelination of anterior roots.
15. Absence of degeneration of nervous tissue.

1. *Familial Incidence.*—In 4 of the 5 cases reported the disease was familial. Oppenheim [14] expressed the belief that amyotonia congenita was not a familial disease. Since his observations, numerous instances in which the disease has been found in more than 1 member of a family have been reported.[15]

The disease has been found in both single amnion [15a,b] and double amnion twins.[16] Gourse [15b] found the disease in identical twins born with a triplet but absent in the triplet.

Reuben [2] reported on a family in which 3 children born in the first four years of married life all showed the disease and all died of pneumonia before the first birthday. Two of our families seem similar to this family of Reuben.

Turner [1a] reported 6 cases in a family having children.

In addition to these reports of the disease a severe form followed by early death is that Benjamin [3] on a family in which there were cases of a mild form of the disease.

In contrast to these reports in which more th 1 member of a family is afflicted, there are a m larger number of cases reported in which bu member of a family has shown the disease.

In answering the inevitable question asked the parents of a child afflicted with amyoto "Can we have a normal baby?" one needs to guarded. The chances of their having a nor baby are good, but they probably run a gre risk than average parents of producing a c

Fig. 11 (case 5).—Cervical portion of the spinal cord, showing almost complete absence of anterior h cells and tenuous anterior roots. Bodian silver impregnation; × 25.

Gurdjian [15c] reported a family having 6 children, 3 of whom had amyotonia congenita, and with amyotonia. For parents who have alre produced 2 afflicted offspring, the outlook fo healthy child is much less bright.

2. *Onset by the Time of Birth.*—Amyoto congenita is apparent at birth. In cases repor by Turner [1a] and Faber [1c] evidences of the ease prior to birth have been obtained from mother, who was said to have stated that f movements had been less vigorous than norm Data on fetal movements obtained from mothers of our patients are inconclusive.

In the cases reported in the literature the servation is universally made that hypotoni was evident soon after birth. In fact, one qu tions the diagnosis in those cases in which onset occurs after a period of good health infancy.

14. Oppenheim, H.: Ueber allgemeine und lokalisierte Atonie der Muskulatur (Myatonie) im frühen Kindesalter, Monatschr. f. Psychiat. u. Neurol. **8**:232, 1900.

15. (*a*) Forbus, W. D., and Wolf, F. S.: Amyotonia Congenita (Oppenheim's Disease) in Identical Twins, Bull. Johns Hopkins Hosp. **47**:309, 1930. (*b*) Gourse, A.: Amyotonia Congenita (Oppenheim's Disease) Occurring in Two of Triplets, J. Pediat. **15**:546, 1939. (*c*) Gurdjian, E. S.: Myatonia Congenita with Particular Reference to Pathology and Familial Tendency, Arch. Neurol. & Psychiat. **24**:52 (July) 1930. (*d*) Lewis, N. D. C.: Heredity in Nervous and Mental Disease, New York, Paul B. Hoeber, 1923, p. 166; cited by Grinker.[4a] (*e*) Benjamin.[3]

16. Gjørup, E., and Schroeder, G. E.: Dystrophia musculaire progressive et myatonie congénitale, Acta pædiat. **18**:211, 1935. Pearce, N. O.: Amyotonia Congenita, Am. J. Dis. Child. **20**:393 (Nov.) 1920.

Hypotonicity of the Skeletal Musculature.—most striking feature of this disease is the otonicity of the muscles. In our cases all the ntary muscles were involved, although those rvated by the cranial nerves were as a rule not cted so severely as those controlled by the . The intercostal muscles were so severely cted as to produce practical immobility of the ax to any but diaphragmatic contraction in f the cases presented here.

he hypotonicity is commented on by all ers on amyotonia congenita. In some cases muscular weakness does not affect all muscles. muscles of the lower extremities are univer- involved.[2] The proximal muscles are usually e affected than the distal ones.[2] Distribution he hypotonicity is symmetric.[2]

Absence of Tendon Reflexes.—Most investi- rs have reported complete absence of tendon exes. However, some have noted a weak le jerk that later disappeared or the tem- ary reappearance of a tendon reflex. In some s there appears to be a return of reflexes in extremity with loss of a regained reflex in ther. Rarely the Babinski sign has been re- ted.

Absence of Electrical Excitability.—In only f our cases were the responses to electrical ulation of the muscles measured. In this no contraction of the skeletal muscles could btained even when the current was increased en times that to which a normal muscle re- nds. There was no reaction to either faradic galvanic current. Such a lack of response has interpreted [6a] as due to a primary defect in muscle itself and not to a degeneration de- dent on interference with the nervous control hanism within the muscle.

Low Blood Creatinine Value.—The blood atinine in case 1 was 0.7 mg. per hundred ic centimeters of blood; in case 4 it was 0.5 per hundred cubic centimeters (normal val- lie between 1 and 3 mg.). Blood creatine determined only in case 3, in which it was nd to be 4.1 mg. per hundred cubic centi- ers. Creatine is a constituent of normal mus- in which it is combined with phosphorus as sphocreatine. This compound breaks down muscle contracts and is built up as muscle re- ers. Most of the creatine in the body is with- he muscles, although its occurrence in other ue suggests that it must have functions in lition to those of muscular contraction.[17]

7. Williams, R. J.: Text Book of Biochemistry, New k, D. Van Nostrand Company, Inc., 1942.

The low value of creatinine in the blood of these patients (cases 1 and 4) reflects the low tide of metabolism taking place in their muscles.

Only Gittings and Pemberton [17a] and Ziegler and Pearce [18] have determined the creatinine excretion in persons with amyotonia. Both found it greatly reduced, as might be expected from the fact that creatinine is the waste product of creatine metabolism.

7. Lack of Involvement of Involuntary Musculature.—In striking contrast to the weakness of the voluntary muscles is the apparent normality of the involuntary muscles. The diaphragm, the intestinal musculature, the myocardium, the bladder, the sphincters and the muscular coats of the blood vessels all gave evidence of normal function during life and at necropsy appeared normal, both grossly and microscopically. This fact has been observed by almost all workers, the only exceptions being an involvement of the diaphragm in 2 cases [19] and of the heart in 1.[15d]

In none of our cases was significant change in the clinical condition of the muscles noted during the period of observation. The muscles became neither weaker nor stronger.

COMMENT

The exact status of amyotonia congenita among the various forms of infantile atrophies is still under discussion. It would seem that this disease must be differentiated from three other disorders: the infantile spinal muscular atrophy of Werdnig-Hoffmann, the infantile types of muscular dystrophies and acute or subacute poliomyelitis occurring in early infancy or even before birth. The immature nervous system differs in its reaction to destructive influence from the nervous system in later years, and consequently the estimation of deficiency versus degeneration is often delicate. For instance, there is a good deal of metabolic fat in the nerve parenchyma; also the glial replacement process is less striking, and, finally, the absence of myelination gives a much less demonstrable picture than does the degeneration of myelin sheaths that have already developed.

There are similar differences with regard to the muscles. Superficially, the mixture of large and small muscle fibers in a given section may be seen in sections from persons with any of the

17a. Gittings, J. C., and Pemberton, R.: Metabolic Observations on Amyotonia Congenita, Am. J. M. Sc. **144**:732, 1912.

18. Ziegler, M. R., and Pearce, N. O.: A Metabolic Study of Amyotonia Congenita, J. Biol. Chem. **42**:581, 1920.

19. (*a*) Wälle, H., and Hotz, A.: Zur Kenntnis der Myatonia congenita (Oppenheim), Jahrb. f. Kinderh. **86**:315, 1917. (*b*) Foot.[1b]

diseases mentioned and even with other conditions, such as partial severing of the nerve supply. While there are variations, it may be stated that in general the small muscle fibers are degenerated in poliomyelitis and in Werdnig-Hoffmann disease and the large ones in the muscular dystrophies. In amyotonia congenita the large muscle fibers are substantially normal, whereas the small ones are immature, resembling normal muscle fibers at the sixth fetal month, before neurotization has been effected. However, this does not exclude either the possibility that the anterior horn cells may have been more or less completely destroyed before such neurotization could have been accomplished or the possibility that adequately developed fibers might have regressed in their development after interruption of their nervous connections. The absence of end plates on the small fibers is of no help in this problem, since it might occur in either condition.

The changes in the spinal cord as reported in the literature are variable from case to case. In the cases reported here they are monotonously similar. Deficiency of large multipolar cells in the anterior horns, with preservation of the sympathetic cells in the lateral columns and of the large rounded cells in Clarke's columns, is the outstanding feature. Decrease in the feltwork of fibers within the anterior horns and striking reduction in the number and size of fibers in the anterior roots have also been described in practically all the cases. Many pathologists have stressed the preservation of such fetal structures as the open central canal with some preservation of its ciliated epithelial lining and the deep grooves along the lateral aspects. However, we have demonstrated identical conditions in normal infants. Authors vary in their description of the anterior horns. Conel,[4b] whose histologic work is exceptionally detailed, has pointed out numerous examples of cells in a state of axonal reaction, and he has established a certain progress in the degeneration of the individual cells to complete degeneration and neuronophagia. Bielschowsky,[20] on the other hand, has called attention to the large number of immature cells, with occasional instances of hypertrophied elements, as indicating a germinal disturbance affecting the development of the cells. Yet Bielschowsky described so-called cell beds, places apparently formerly occupied by multipolar elements which are either blank or filled in with a delicate glia reticulum, and he spoke repeatedly of *Ausfall,* indicating a progressive degeneration. He further admitted the likelihood of progressive deg eration of the cells that are shrunken and de stained. To him, amyotonia represented a order in which there are indications not onl abiogenesis but of selective vulnerability of developing nerve cells.

Spiller [5a] and Bielschowsky [20] apparently h been the only investigators to find a deficienc the motor cells of the precentral cortex, and s eral authors have stated specifically that th cells are normal. To make matters more c fusing, Spiller found no significant changes the spinal cord. Greenfield and Stern [21] w inclined to exclude Spiller's case from the c gory of cases of amyotonia congenita becaus the late onset with lack of alertness, and the that in response to a pinprick the child withd the limb "with considerable force." Bielsch sky's case 2 is more acceptable, the weak having been present at birth. He wrote, " development of the giant pyramidal cells of [gyrus centralis anterior] does not reach degree expected at this age. They have decide smaller cell bodies, poorly developed basal d drites, and in the cell stain do not show cle the stichochrome arrangement of the chrom philic granules."

This observation of Bielschowsky's agrees c pletely with ours and seems of the utmost imp tance in distinguishing amyotonia congenita f the other disorders. If it can be shown that th is failure of development of the upper motor n ron, both cell body and corticospinal axon, al with that of the lower motor neuron, the case a congenital deficiency of the whole motor ap ratus would seem to be well established. T amyotonia congenita would become the coun part of amyotrophic lateral sclerosis, in wh both upper and lower motor neurons are und going degeneration simultaneously. Apparen the precentral cortex has not been investiga often enough in amyotonia congenita and all disorders to ascertain whether this feature i valid criterion in differential diagnosis. Con cases, in which the precentral cortex was int and the motor cells of the bulbar nuclei and spi cord showed varying degrees of degenerati might possibly come more properly under heading of cases of infantile spinal muscu atrophy.

The confusion between amyotonia congen and infantile muscular dystrophy has been where better presented than by Turner.[18]

20. Bielschowsky, M.: Ueber Myatonia congenita, J. f. Psychol. u. Neurol. **38**:199, 1929.

21. Greenfield, J. G., and Stern, R.: The Anatom Identity of Werdnig-Hoffmann and Oppenheim Fo of Infantile Muscular Atrophy, Brain **50**:652, 1927.

ase present in 6 of the 13 children of a family first classified as amyotonia congenita, and r was reclassified muscular dystrophy. This probably because of the dictum of Oppenn himself, who stated that the muscles were k but not atrophic. Every pathologic study amyotonia congenita has shown the falsity his concept. The muscles are always undereloped, but this is apt to be concealed in ncy because of the heavy layers of subcuous fat giving firmness as well as bulk to the ic limbs. It is our belief that Turner's cases e instances of amyotonia congenita (the her could tell before birth which of her chiln would be born paralyzed, because of the ence of fetal movements) in which the dency was not sufficiently pronounced to cause th at an early age. As the children grew out nfancy, the absence of muscular development me manifest as soon as the fatty panniculus absorbed.

Amyotonia congenita is compatible with life in inority of cases. Improvement has been reted but never proceeds to a normal extent. lsen [22] reported a case in which the deformities e been almost fantastic. In this respect, amyoia congenita may be confused with fetal or natal poliomyelitis, although in the latter dise there is not likely to be the same symmetry as which characterizes amyotonia congenita. rthermore, the occurrence of an acute illness in reviously active infant or in its mother shortly re delivery may establish the diagnosis. ere is no difficulty in establishing the cause of paralysis if death occurs in the acute stages, reported by Tuthill and Levy,[23] since the inflammatory phenomena are striking. It seems probable that there might be more difficulty in establishing the diagnosis in a case of recovery with death later from intercurrent disease.

Werdnig-Hoffmann disease begins characteristically in the second half of the first year of life in a previously healthy infant, but it may have its inception earlier and in some instances it may be congenital. One instance has been reported in which it was observed that a child was paralyzed at birth while its twin became paralyzed at about the age of 6 months. Pathologically, in Werdnig-Hoffmann disease there are indications of degeneration reaction, sometimes inflammation and reparative gliosis. These phenomena are slight or absent in cases of amyotonia congenita.

SUMMARY

Five cases of amyotonia congenita are reported which have the following outstanding features: (1) familial incidence; (2) onset by time of birth; (3) hypotonicity of all skeletal musculature, except those supplied by bulbar nuclei; (4) absent reflexes, absent electrical excitability of muscles; (5) low blood creatinine; (6) no clinical improvement; (7) death from bronchopneumonia in infancy; (8) embryonic type of skeletal musculature without evidence of degeneration; (9) paucity of anterior horn cells; (10) decreased myelination of anterior roots; (11) absence of large multipolar Betz cells in the motor cortex.

Amyotonia congenita is thought to originate from a developmental defect which affects both the giant pyramidal cells of Betz in the motor cortex and the anterior horn cells of the spinal cord with resulting hypoplasia of the muscles.

Photomicrographs were taken by the Army Medical Museum, Colonel J. E. Ash, Curator.

2721 Connecticut Avenue.
4501 Linnean Avenue, N. W.
3821 Woodley Road, N. W.

2. Nielsen, J. M.: Myatonia Congenita of Oppenn: Report of Unique Case, Am. J. Dis. Child. **35**:82 .) 1928.

. Tuthill, C. R., and Levy, M. G.: Amyotonia: ort of Case with Histologic Observations, Am. J. Child. **41**:591 (March) 1931.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

INFANT FEEDING IN A RATIONED ERA. NORMAN M. MACNEILL, Pennsylvania M. J. **47**:209 (Dec.) 1943.

This article should do much to focus greater attention on the possibility of breast feeding for larger numbers of infants than receive it at present. The author points out that far too often breast feeding is lacking because of insufficient interest on the part of physician, nurse or attendant. Too early introduction of solid foods also tends to produce a decrease or cessation of breast milk. The author favors introduction of cereal at the fifth month and vegetables at the sixth month. He also believes that freshly prepared vegetables are better than the canned variety. The indiscriminate use of vitamins is deplored, C and D being the only ones routinely required. It is pointed out that the regimen indicated not only is better for the baby but releases canned milk and vegetables for the war effort.

LESLIE, Evanston, Ill.

A NUTRITIONAL SURVEY OF SCHOOL CHILDREN IN OXFORDSHIRE, LONDON AND BIRMINGHAM. MILA I. PIERCE, Proc. Roy. Soc. Med. **37**:313 (May) 1944.

In the summary of her paper, the author makes the following statements: 1. The general health rating of the children was best in the schools of Oxfordshire; the schools of London rated second, the villages third and the schools of Birmingham lowest. 2. The levels of ascorbic acid were within normal range only in the villages. The availability of new potatoes and garden stuffs accounted primarily for the difference. 3. Indication was found that a correlation exists between levels of ascorbic acid in the blood of a given group and the general health of that group. 4. A meal at school did not raise the levels of ascorbic acid in the blood to that of children who did not take the meal. Interpretation of the finding necessitates knowledge of the home conditions of the two groups and more information regarding the vitamin content of the food as served in the schools. The use of foodstuffs of high vitamin C content is to be encouraged for both school and home menus. 5. The serum protein levels were lowest in the age group of 5 to 7 years and highest in the age group of 11 to 13 years. No evidence of protein deficiency was found. 6. Levels of hemoglobin were higher for the school children of all three districts than the levels recently reported for London and Edinburgh. 7. Physical examinations gave a more accurate measure of the health status of the children than did the laboratory methods employed in this survey. In districts where the school meal must necessarily be limited, selection by physical standard rather than by an economic one seems desirable.

WILLIAMSON, New Orleans.

DANGERS OF STARVATION AND UNDERFEEDING IN INFANCY. L. VELASCO BLANCO, Arch. am. de med. **18**:13 (Jan.) 1942.

The author points out the disastrous effects of underfeeding and starvation in breast-fed and bottle-fed infants. He discusses the most frequent causes, stre the importance of anorexia in both groups, of di suction in breast-fed babies and of fear of food in ance in artificially fed infants. The occurrence of rhea in undernourished babies is considered respo for misleading interpretations. The discussion is ited to quantitative underfeeding.

ABALLI, Habana, Cu

BLOOD CELLS IN "DYSTROPHIC" EDEMA. C. T UMAÑA, Bol. Soc. cubana de pediat. **15**:775 (1943.

The author prefers the term dystrophic edema t more commonly used name "nutritional" edema. points out that in a report of cases of this cond by Valencia, there was a group of patients wh well as having edema, presented symptoms of pur He confirms the reports of others that hypochr anemia occurs in all cases of "dystrophic" edema points out that protein is essential in the formati hemoglobin, as demonstrated in Whipple's experi on dogs. He reports on 18 patients with "dystro edema, 7 of whom had thrombopenic purpura. of the patients died, indicating that purpura is evi for a very poor prognosis. In patients who re the disappearance of purpuric signs and the e parallel the increase in blood proteins and hemogl

KEITH, Rochester, Mi

Vitamins; Avitaminoses

ACIDOTIC TYPE OF ACUTE BERIBERI IN THE NU INFANT. A. DE LOS HEROS, Bol.. Soc. cuban pediat. **16**:94 (March) 1944.

The author gives a general discussion of the sub with a review of the literature, and describes 8 c with reference to the symptoms, diagnosis, prog and treatment. The data are given in tabular f All the patients had tachycardia, cyanosis, perip vascular collapse and oliguria. At least 4 of the in had roentgenographic evidence of cardiac enlarge All had typical facies, pallor and edema of the ch contrasting with the cyanosis of the lips. The b were 2 to 4 months old, and their mothers all grossly deficient diets. Thiamine chloride, 50 mg., intravenously, followed by injection of smaller am intramuscularly, caused disappearance of the symp in a few hours.

KEITH, Rochester, Mi

TREATMENT OF RICKETS WITH SINGLE DOSES OF V MIN D. A. BAHIA, A. RIBEIRO, U. FREITAS G. CALDAS, Pediat. e puericult., Bahia **12**:36 (1942.

The authors believe that rickets is more prev in Bahia than was previously supposed. It is not more frequent among Negroes than among white sons. In 20 cases vitamin D in single massive was successful in curing symptoms in twenty-on ninety days.

SANFORD, Chica

giene; Growth and Nutrition; Public Health

TERNAL MORTALITY AND INFANT MORTALITY IN MONTREAL. A. GROULX, Union méd. du Canada **72:** 413 (Dec.) 1943.

he director of the Health Department of Montreal ents comparative figures of maternal and infant tality. In 1900-1904 the infant mortality rate was 9 per thousand births; in 1942 it had fallen to 57.7 thousand. The principal causes of the 1,190 infant hs in 1942 were prematurity (24.45 per cent), rhea (12.77 per cent), malformations (12.61 per), pneumonia (11.51 per cent) and otitis and mas- itis (8.74 per cent).

large factor in this reduction is the establishment hild welfare stations and well baby clinics, together extensive education programs. Of particular value reducing the mortality from diarrhea (64.8 per sand in 1920-1924, 7.8 per thousand in 1942) has the purification of the water supply and the milk rol campaign.

DAFFINEE, Melrose, Mass.

Prematurity and Congenital Deformities

GOYLISM: REVIEW OF LITERATURE WITH REPORT OF TWO CASES. L. A. LURIE and S. LEVY, Am. J. M. Sc. **207:**184 (Feb.) 1944.

both cases of gargoylism the children presented characteristic skeletal deformities, marked enlarge- of the spleen and liver, umbilical hernia and lemindedness. Laboratory tests of hepatic function abnormal values, showing definite damage to the . Roentgenograms of bones showed marked de- mental retardation as well as structural changes. the authors' cases there was no consanguinity; her were the parents mentally retarded.

HENSKE, Omaha.

USUAL CONGENITAL ANOMALIES OF THE LUMBO-SACRAL SPINE (SPINA BIFIDA) WITH A REPORT OF THREE CASES. J. M. MEREDITH, J. Nerv. & Ment. Dis. **99:**115 (Feb.) 1944.

hree unusual cases of lumbosacral spina bifida are ussed.

In a 6 year old girl with spina bifida occulta the f disorder was referable to the bladder. Explora- showed adherence of a number of strands of the la equina to the dura at the level of the second al vertebra.

In a 13 year old girl with a cholesteatoma a le meningocele immediately caudad to the tumor been removed ten years previously.

In a man aged 32 who presented symptoms of lvement of the cauda equina the conus medullaris adherent to the dura at the level of the second al vertebra.

ll 3 patients showed decided improvement after sur- l repair.

JAHR, Omaha.

NDRODYSTROPHIA. MAXWELL P. BOROVSKY and J. ARENDT, J. Pediat. **24:**558 (May) 1944.

n unusual case of congenital maldevelopment was d in a newborn infant. Attention was first directed he bones by the contractures of both knees and the overy that extensive calcification was present within capsules of both knee joints. Further roentgeno- hic studies revealed stippled, shotlike densities at wrists, ankles, shoulders and knees.

The name "chondrodystrophia calcificans congenita" was applied to this condition by Gerard Raap. Similar cases have been reported, chiefly in the roentgenologic literature.

Some authors attribute this maldevelopment to hypothyroidism, a condition which did not prevail in the present case. Resolution of the calcium deposits in the knees and the appearance of more normal epiphyses, where the stippled areas were originally present, were noted at the age of 1 year. Thyroid was not administered.

This infant and 2 of the other patients reported to have this condition also had congenital lesions of the heart.

BOROVSKY, Chicago.

TOTAL TRANSPOSITION OF THE VISCERA IN THE CHILD. T. SEMINARIO VERA, Rev. Hosp. d. Niño **6:**167 (June) 1944.

The author reports 2 cases of situs transversus, 1 in a girl of 5 years and the other in a girl of 2 years. Roentgenograms of the chest and the intestinal tract are given in 1 case and of the chest only in the other. Electrocardiograms taken in the first case are shown. There is a brief discussion of reports in the literature.

KEITH, Rochester, Minn.

Acute Contagious Diseases

BLOOD DIASTASE VALUES IN MUMPS AND MUMPS PANCREATITIS. SAMUEL ZELMAN, Am. J. M. Sc. **207:** 461 (April) 1944.

Values for blood diastase were determined in a series of 89 patients with mumps on admission to the hospital and on discharge. Seventy-three per cent had values above normal on admission, and 9 per cent, on discharge. Three per cent had subnormal values on admission, and 20 per cent, on discharge. Fifteen per cent of this series showed evidence of pancreatitis at some time during the course of the illness.

Among the patients who later had pancreatitis the percentage of increased diastase values on admission was especially high. Studies intended to illuminate the possible role of the pancreatitis in producing these values did not prove feasible in the circumstances of the study.

HENSKE, Omaha.

SALT METABOLISM IN POLIOMYELITIS. JAMES F. RINEHART, J. Nerv. & Ment. Dis. **99:**825 (May) 1944.

Studies on serum chlorides and the packed volume of red blood cells in patients with poliomyelitis early in the disease show depletion of salt and hemoconcentration. The author suggests that the development of the disease in so many instances following muscular exertion and its predominance during the season in which perspiration is greatest may be more than a coincidence. The possibility of a relation between water and salt metabolism and poliomyelitis is worthy of further investigation.

JAHR, Omaha.

MEDICAL PROGRESS: THE DIFFERENTIAL DIAGNOSIS OF CHICKENPOX AND SMALLPOX. CONRAD WESSELHOEFT, New England J. Med. **230:**15 (Jan. 6) 1944.

An attack of chickenpox or smallpox tends to confer a lasting immunity. In general it may be stated that prodromal symptoms are absent or slight in chickenpox and severe in smallpox. The fact is that since chickenpox usually occurs in childhood and is generally mild,

prodromes are rarely present. The prodromal symptoms of a severe form of smallpox may begin three days before the eruption. The outstanding complaint is backache, which is usually lumbar in children; it is an excruciating agony, accompanied with fever, chills, sweats and vomiting. Hoyne has noted salivation, especially in Negroes.

The eruptive stage in both these diseases is probably the result of a violent antigen-antibody reaction in the skin. The inflammatory reaction may spread beyond the edge of the vesicle in the form of an erythematous area at the base. This is much more conspicuous in chickenpox than it is in smallpox and affords an important point in differentiation. The irregularity of the corona in the lesion of chickenpox is often reflected in the shape of the vesicle itself. The vesicle of smallpox tends to remain round, but sometimes as these lesions run together their edges have a crenated appearance.

For chickenpox the temperature curve reaches its highest point as the eruption comes into full bloom, on or about the second day, after which it tends to fall to normal, either abruptly or within about forty-eight hours. The temperature curve for smallpox is quite different. In the first place, it is diphasic, and, in the second, it is protracted. As the eruption appears or is about to appear, the patient experiences a short phase of apparent improvement. Then the temperature begins to rise gradually, rarely abruptly, through the vesicular stage, with a sharp increase marking the onset of the pustular stage. From that time there is a long, high plateau, lasting two or three weeks. In chickenpox the first vesicles appear suddenly—within two or three hours—and these are followed by others cropping out here and there in an irregular manner. Thus, at the end of twenty-four hours there are often lesions in all stages of development over a given area. This condition becomes more prominent at the end of forty-eight hours. Itching of the lesions of the skin may be severe.

The protracted course of events in smallpox begins with the severe and prolonged prodromal period and is followed by a brief period of lowered temperature and relative comfort. The first signs of the eruption then appear, usually during the third or fourth day of the acute illness. In general, all the lesions can be said to come out together, and they thus tend to be at the same stage.

GENGENBACH, Denver.

ELECTROMYOGRAPHIC STUDIES OF MUSCLE DYSFUNCTION IN INFECTIOUS POLYNEURITIS AND POLIOMYELITIS. MARY BRAZIER, ARTHUR L. WATKINS and ROBERT S. SCHWAB, New England J. Med. **230**:185 (Feb. 17) 1944.

Electromyographic studies revealed the following similarities of muscular dysfunction associated with infectious polyneuritis and poliomyelitis: Muscular tenderness and paresis are characteristic of both diseases, and the electrical abnormalities present with both conditions are correlated with weakness rather than with sensitivity. Partially paralyzed muscles on stretching show hyperirritability, which can be relieved by hot fomentations. Even at rest, paretic muscles are hyperirritable, discharging electrical potentials characteristic of regenerating motor units. Reciprocal innervation is frequently disrupted in polyneuritis and poliomyelitis, with resulting simultaneous activation of opposing muscles—this abnormality is probably secondary to painful motion. The disorganization of reciprocal innervation is not so severe in polyneuritis as in poliomyelitis, for the simultaneous activation of opposing muscles in the form disease is not characterized by synchrony of compon discharges.

GENGENBACH, Denver

MENINGOCOCCAL MENINGITIS. RALPH R. MEYER, N England J. Med. **230**:452 (April 13) 1944.

Thirty-three cases of meningococcal meningitis w encountered in the contagious disease service of station hospital at Camp Grant, Ill., between Januar and July 3, 1943. Four cases are presented in det including 1 in which hemorrhage into the adrenal gla (Waterhouse-Friderichsen syndrome) was a seri complication. All the patients were adults between ages of 18 and 34 years.

The symptoms, physical signs, laboratory findings treatment are presented. The therapeutic agents e ployed were sulfadiazine, sulfathiazole and polyva antimeningococcic serum. In this unselected series cases there were no deaths.

GENGENBACH, Denver

PROBLEMS IN EARLY TREATMENT OF POLIOMYELI J. WRIGHT, New York State J. Med. **44**:67 (Jan 1944.

There is a widespread misconception regarding results that can be accomplished by the sister Ke treatment. Kenny has made a valuable contribut to the therapy in the acute stage, the early recogni of spasm and the intensive treatment of spasm by me of hot fomentations. The care of patients must individualized and any standard method varied to m the different conditions. Measures that have been fo valuable in former times should not be hastily discar for newer methods.

AIKMAN, Rochester, N. Y

Acute Infectious Diseases

A CASE OF HISTOPLASMOSIS IN AN INFANT W AUTOPSY. HANS G. SCHLUMBERGER and ALLEN SERVICE, Am. J. M. Sc. **207**:230 (Feb.) 1944.

The authors describe the case of a 7 week old ini with signs of anemia, splenomegaly and hepatomeg The diagnosis of histoplasmosis followed discovery the parasite in material obtained by splenic punct and was verified by subsequent culture and ani inoculation.

HENSKE, Omaha

RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE LOS ANGELES CHILDREN. DAVID B. DAVIS SIDNEY ROSIN, J. Pediat. **24**:502 (May) 1944.

The cases of 157 children with rheumatic dise admitted to the Los Angeles County Hospital ove five year period are analyzed and discussed by authors. The following findings are emphasized:

1. The relatively low incidence (0.69 per cent) rheumatic disease as determined by this survey is c sistent with the findings of similar studies carried in other cities with subtropical climates.

2. Chorea seems to occur with much less freque (15.6 per cent) in this area than in eastern popula centers.

3. No significant variation in seasonal incidence noted.

4. An analysis of temperature, rainfall and rela humidity permits no correlation between these fac and the incidence of the disease in this area.

5. Familial incidence in the cases studied was ligible.

Two thirds of the patients were born and raised this community. Almost 80 per cent of the patients n outside California lived in the Los Angeles area r one year before the onset of rheumatic disease. ese factors tend to discredit the commonly held ief that the majority of persons with rheumatic ection encountered in Los Angeles are migrants m eastern or northern states.

The mortality in the series was 9.5 per cent. ief summaries of all fatal cases are presented.

GENGENBACH, Denver.

E CARRIER STATE IN SONNE DYSENTERY. J. GORDON HAILWOOD, Brit. M. J. **1**:806 (June 17) 1944.

Carrier states in Sonne dysentery are extremely rare. e appearance of Sonne dysentery in the British y at various places throughout the country led the hor to investigate a rather severe outbreak of the ease that occurred in an artillery regiment in July d August 1943. This regiment had about 900 men, d 292 had diarrhea. The stools of 81 of the latter re positive for Shigella dysenteriae Sonne. It was nd in this particular camp, which was limited and off from all outside communications, that no one the permanent staff had dysentery. It was also ed that the food prepared for this group was enely separate from that for the rest of the camp. er a good deal of searching and many cultures of ols of all the members who had had any diarrhea d several cultures of specimens of all the other pernel of the cook houses, it was found that one of the ks was the carrier. He had no symptoms during attack of diarrhea studied, but a little over one r prior to this outbreak he had had a typical attack dysentery. Culture of his feces revealed a heavy ection with the bacillus of Sonne dysentery. It was nd that this man had visited and had helped in all other cook houses except the cook house of the manent staff. Removal of this man and of other mbers of the cooking staff who had a positive stool S. dysenteriae Sonne immediately stopped the outak. The author states that the so-called symptomless carrier of Sonne dysentery is common but that a tory of diarrhea at some time in the past can usually obtained.

BIRDSONG, Charlottesburg, Va.

LARIA IN CHILDHOOD. L. VELASCO BLANCO and D. SILBERBERG, Arch. am. de med. **18**:33 (April) 1942.

The authors present a case of malaria in a 10 year girl who had a recurrence a year after receiving nine therapy and responded quickly to treatment h a mixture of quinacrine hydrochloride and pamaine naphthoate.

ABALLI, Habana, Cuba.

MAN RABIES AT THE CHILDREN'S HOSPITAL, LIMA, PERU: REPORT OF CASES. GUILLERMO FILOMENO, Rev. Hospital d. Niño **6**:167 (June) 1944.

The author reports 3 fatal cases in children, all of om were bitten about the face. Autopsy in 2 cases wed definite rabies. None of the patients was ated with vaccine. A general discussion of rabies ows, and a plan for treatment and prophylaxis is lined.

KEITH, Mayo Clinic.

INVESTIGATION OF KALA-AZAR AND SAND-FLY INCIDENCE IN AN ENDEMIC KALA-AZAR AREA IN THE WESTERN PART OF SZECHUEN. P. C. HOU, Chinese M. J. **61**:279 (Oct.-Dec.) 1943.

An investigation in a small village revealed a 4 year boy who had kala-azar with typical clinical symptoms and, on splenic puncture, Leishman-Donovan bodies. Sand flies were present in the home. The child had never visited places known to have this disease, though it was reported in neighboring villages. Sand flies were present within and without the borders of the town. Another boy 4 years of age was found to have the febrile disease, with enlargement of the abdomen for three months. Sand flies were present in the house. Another case was that of an 18 month old child in the same small city.

The author states that the climate, with its dryness and small rainfall, is suitable for the breeding of sand flies. Wherever kala-azar was found, sand flies were present.

NEFF, Kansas City, Mo.

Chronic Infectious Diseases

DEVELOPMENT OF PULMONARY TUBERCULOSIS IN CONGENITAL HEART DISEASE. OSCAR AUERBACH and MARGUERITE G. STEMMERMAN, Am. J. M. Sc. **207**: 219 (Feb.) 1944.

The authors studied 13 patients who had congenital heart disease and acquired pulmonary tuberculosis, on 7 of whom postmortem examination was performed. The most common congenital defect was pulmonary stenosis, which was present in all patients studied at autopsy, implying a certain predisposition of patients with this lesion to tuberculosis.

A composite picture of the typical case, including the clinical, physiologic and pathologic features, is presented. From this material one may conclude that the pulmonary tuberculosis runs a course typical of that disease, irrespective of the cardiac lesion. The function of the defective cardiac system is affected unusually little by the superimposed infection of the respiratory tract.

Pneumothorax induced in 5 of the patients did not lead to congestive heart failure in any instance. The importance of other surgical forms of collapse therapy is discussed.

HENSKE, Omaha.

RADIATION THERAPY FOR OBSTRUCTING TUBERCULAR HILAR LYMPH NODES. KAL FREIREICH, Am. Rev. Tuberc. **49**:31 (Jan.) 1944.

The favorable results obtained in the treatment of tuberculous enlargement of lymph nodes with roentgen rays suggests that involvement of the hilar nodes might react favorably to such therapy. A good response was obtained in the case reported, in which the roentgenogram and bronchoscopic examination revealed bilateral compression of the main bronchi by enlarged mediastinal lymph nodes. As a result gradually increasing obstructive symptoms and dyspnea developed. These symptoms were relieved by three roentgen ray treatments. Not only were the subjective symptoms relieved, but later roentgenographic examinations revealed no evidence of compression of the bronchi.

EUGENE H. SMITH, Ogden, Utah.

ANTITUBERCULOUS VACCINATION WITH BCG. J. A. BAUDOUIN, Union méd. du Canada **72**:826 (July) 1943.

A total of 946 children were under observation, of whom 438 received BCG vaccine. The nature of the tuberculous contact was approximately the same in the two groups. Ninety-one children died—34 from the vaccinated group and 57 from the unvaccinated group. The mortality rate therefore was 77.5 per cent in the vaccinated group, as compared with 112 per cent in

the unvaccinated group. Tuberculosis accounted for 23 per cent of the deaths in the vaccinated group and 44 per cent in the unvaccinated group. The difference was most striking in the first three years of life.

Tuberculosis developed in 65 of the vaccinated children and in 166 of the unvaccinated children.

Baudouin stresses the safety of this form of protection and urges that it be used universally.

DAFFINEE, Melrose, Mass.

MASSIVE PULMONARY ATELECTASIS OCCURRING IN THE COURSE OF A PRIMARY TUBERCULOUS INFECTION. G. CARDELLE, F. BORGES and R. PEREIRAS, Bol. Soc. cubana de pediat. **16**:85 (March) 1944.

A boy of 19 months, one of whose grandparents had tuberculosis, had fever and cough for one month. The Mantoux reaction was positive, and gross posterior mediastinal adenitis, with signs of obstructive emphysema of the left lung, was present. Two days later roentgenograms showed massive atelectasis, pulling of the mediastinum to the left and collapse of the left lung. Bronchoscopic examination on his admission showed reduction in the size of the left main bronchus, congestion and edema of the mucosa and much mucus. Diagnostic pneumothorax was carried out. Fifteen days later reexpansion was considerable. Six months after his admission roentgenograms of the chest showed no pleural or pulmonary changes.

The authors consider this case one of atelectasis due to endobronchial changes.

The report closes with a good discussion of the cause, diagnosis and prognosis. The prospect for recovery is said to be good. Artificial pneumothorax appears to be effective.

KEITH, Rochester, Minn.

TUBERCULOSIS: INCIDENCE AMONG CHINESE CHILDREN. ANNIE V. SCOTT, Chinese M. J. **61**:117 (April-June) 1943.

The author summarizes the positive findings in tuberculin tests on 2,937 city children and 1,787 country children. The statistical results show that there is a significant sex difference in both groups: The percentage of positive reactions for girls from the country and the city together was 48, while that for the boys was 42.2.

NEFF, Kansas City, Mo.

TUBERCULOSIS OF THE FLAT BONES OF THE VAULT OF THE SKULL. C. M. MENG and Y. K. WU, Chinese M. J. **61**:155 (April-June) 1943.

The authors discuss the etiologic factors of sex and age. Tuberculosis of the skull has previously been considered a relatively rare disease, but in countries where tuberculosis is still common this is not true. Where the social and economic standards of people are low the disease is prevalent. In China the general morbidity rate for tuberculosis is high, and osseous involvement is common. One would expect, therefore, that the flat bones of the skull would not escape infection. The authors discuss the factors of trauma, the associated tuberculous lesions, the pathogenesis, the number, location and types of lesions, the clinical manifestations and the diagnosis. Forty cases are analyzed. The incidence of the disease is highest during childhood and adolescence; the invasion of the skull is nearly always secondary to active or latent lesions elsewhere. Other flat bones may be involved at the same time. Clinically the lesions usually resemble a painless cold abscess or sinus. Roentgenographic examination may help in the diagnosis in some cases; bi and aspiration may be valuable. All patients sh be given general antituberculosis treatment.

NEFF, Kansas City, M

Diseases of Blood, Heart and Blood Vessels and Spleen

RHEUMATIC PERICARDITIS WITH EFFUSION IN PATIE UNDER TWO YEARS OF AGE. GERARD N. K J. Pediat. **24**:514 (May) 1944.

Two cases of pericarditis with effusion in chil under 2 years of age are reported in which the co tion was probably of rheumatic origin. The onse the symptoms agrees with the conclusion of McIn and Wood that the clinical picture of rheumatic dis in the age group below 3 years is more often tha a general infection than that of a specific disease en

The first patient was seen on the third day o acute illness with no subjective symptoms of car involvement, only those of an acute infection. classic signs of pericarditis with effusion were covered on routine physical examination. There a moderate rise in temperature, the elevation persis in the evening for three weeks. All clinical evid of effusion and cardiac involvement had disappeare that time. At no time was there any suggestion septicemia. The patient remained at home, and t were no laboratory tests to confirm the purely cli impression of rheumatic pericarditis.

The second patient was hospitalized on the se day of her illness. The onset of the illness was a Dyspnea appeared on the second day. Pericarditis effusion was diagnosed on the sixth day of the ill Cultures of blood taken on the second and sixth of the illness were sterile. Sulfadiazine was give adequate dosage for six days, without benefit. cardiac embarrassment necessitated the use of oxy continuously and pericardial taps on the sixth and thirteenth day of the illness. The temperature bec normal on the fifteenth day. The sedimentation on the twenty-eighth day was 25 mm. in one h two weeks after the temperature became normal. sedimentation rate was 14 mm. two months after onset, when all other evidence of infection had di peared.

Cardiologists, especially pediatric ones, will prob disagree with this diagnosis, as rheumatic pericar is usually part of a pancarditis, with severe car damage. The course, the absence of any evidence septicemia and the definite laboratory findings in second case exclude sepsis, the only other possibi

KROST, Chicag

ACUTE PERICARDITIS DUE TO STREPTOCOCCUS VIRID M. D. HARGROVE, New Orleans M. & S. J. **96** (April) 1944.

The author reports recovery in a case of acute p carditis due to Streptococcus viridans. The treatm used was aspiration of the pericardial cavity and anilamide.

BERKLEY, Beverly Hills, Cal

BONE-MARROW TRANSFUSION IN INFANTS AND C DREN: INTRODUCING A SPECIALLY DESIGNED NE JANET D. GIMSON, Brit. M. J. **1**:748 (June 3)

This article is helpful in that it introduces a spec designed needle and apparatus for use in transfus into bone marrow. The advantageous features of needle are as follows: 1. The needle is light. 2. distance between the mount and the flange is s

The flange is immovable, so that the extra weight screw mechanism is avoided. 4. Each needle has own stylet, and there are needles of various sizes. There is one handle for the set, which can be screwed the stylet in order to get a good grip during in- ion of the needle. 6. The right-angled adaptor pro- s that the tubing can lie parallel to the leg instead ying or projecting perpendicular to the bone. This elpful with small children. The technic for the use his apparatus is merely surgical. The skin and osteum are anesthetized with a 1 per cent solution procaine hydrochloride. With the needle at right les to the plate of bone, i. e., pointing poster- rally with reference to the leg itself, the needle stylet are inserted with a firm, twisting motion, force the needle into the marrow cavity. When the et is withdrawn, a small amount of marrow may up or be sucked into the syringe. Any of the al transfusion fluids may be given in this way— e solution, Hartmann's (lactate-Ringer) solution, od, serum or plasma. BIRDSONG, University, Va.

NSFUSION OF CELL CONCENTRATES. A. L. GOODALL, Glasgow M. J. **23**:161 (June) 1944.

hen plasma is being obtained for other purposes, a waste to discard the cells. The author used cells suspended in saline solution in treatment of mia. He feels that such a suspension is superior whole blood in some cases.

SNELLING, Toronto, Canada.

UE OF RETROGRADE AORTOGRAPHY FOR DIAGNOSIS OF COARCTATION OF THE AORTA. A. CASTELLANOS, R. PEREIRAS and D. CAZAÑAS, Arch. de med. inf. **11**:9 (Jan.-March) 1942.

he authors report the case of a 6 month old child presented from birth a slight cyanotic condition. re were a mild systolic murmur in the mesocardiac on and moderate hepatomegaly.

he teleroentgenogram showed certain qualitative and ntitative modifications of the cardiac shadow. All diameters were increased, the transverse diameter g the most prominent (6.5 cm.). The transverse eter of the vascular pedicle was decreased, with nce of the first arch on the left margin.

he angiocardiogram demonstrated an interauricular an interventricular communication, with total trans- ion of the large vessels and with the aorta force- lodged to the right and resting on the right chus.

he retrograde aortogram in both exposures showed besides the deviation of the aorta to the right, e was coarctation of the aorta. Such a diagnosis ld have been impossible if this technic had not been loyed.

or the first time in the history of roentgenology and diology the authors have demonstrated that it is ible to obtain the radio-opacification of the heart and arge vessels by the injection of a contrast substance the peripheral vessels (arteries and veins).

ngiocardiography has been demonstrated to be of ordinary value in the diagnosis of congenital diopathies, as the work of the authors and experi- ts in Boston and California have proved.

he authors previously reported on retrograde, more monly known as countercurrent, aortography (*Rev. na de cardiol.* **2**:187 [April] 1940) as a method for diagnosis of stenosis of the ductus arteriosus; it is of value in cases of coarctation. The method also reveals any anomalies of the larger arterial trunks that come from the aortic arch. In this case there was transposition. BRIBIESCA, Zamora, Mich., Mexico.

CHRONIC MALIGNANT FAMILIAL NEUTROPENIA WITH ATYPICAL GRANULATION OF THE LEUKOCYTES. A. BÉGUEZ CÉSAR, Bol. Soc. cubana de pediat. **15**:900 (Dec.) 1943.

Certain cases are reported in which the condition was sufficiently distinctive in its characteristics to be given the name chronic malignant granulocytopenia. The disease is characterized by albinism, attacks of sepsis of undetermined origin, nystagmus, leukopenia, granulocytopenia, monocytosis and lymphocytosis and the presence of atypical granules in the leukocytes. The disease, present in several members of a family, satisfies Charcot's postulates and can be classified as familial, and it has recessive mendelian characteristics. The author states that the protoplasmic inclusion bodies in the leukocytes have not previously been demonstrated and that his cases represent a new hematologic picture. KEITH, Rochester, Minn.

MASSIVE EOSINOPHILIA, LEUKEMOID IN TYPE, INFECTIOUS IN ORIGIN AND REGRESSIVE IN EVOLUTION—A NEW CLINICAL ENTITY. T. VALLEDOR, A. FERNÁNDEZ BALTRONS and J. CORNEJO, Bol. Soc. cubana de pediat. **15**:923 (Dec.) 1943.

The authors have studied in detail 9 patients (3 adults and 6 children) with what they believe to be a new clinical entity. The syndrome consists of protracted fever; catarrhal manifestations; generalized adenopathy; almost always moderate splenomegaly; leukocytosis (count of 30,000 to 70,000), and pronounced eosinophilia, with more than 50 per cent eosinophils in most cases and over 80 per cent in some. In the first months of the illness, and coincident with the high leukocyte level, a reticular pattern was observed in the roentgenograms of the lungs in every case, and in several instances a micronodular pattern of the lungs was present, which subsided with the clinical improvement. The leukocytosis is due to the high eosinophilia, the majority of the eosinophils being adult forms. The number of neutrophils and lymphocytes is low but increases relatively as improvement occurs. There is no definite change in the erythrocytes, or there may be slight anemia. The eosinophilia is present in the bone marrow; again, adult forms prevail. It is present in the lymph nodes as well. The disease tends to regress and may disappear in from one to two years. The febrile period lasts from two or three weeks to several months.

The eosinophilia is not due to intestinal parasitism or to an allergic state. In the differential diagnosis the authors consider parasitic disease, allergic manifestations, dermatoses, hydatidosis, trichinosis and eosinophilia in the initial stages of myelogenous leukemia, as well as familial eosinophilia. The disease is not leukemia, as all 9 patients recovered and 4 of them remained well after seven to nine years. It is felt that the disease is an infectious process, as nuclear inclusions and spheroid protoplasmic inclusions are found in macrophages of the histoplasmic type suggesting the possibility of a filtrable virus or a low protozoon as the etiologic agent. Bass, in 1941, reported 3 similar cases in children, and Weingarten, of Calcutta, in 1943, reported 81 cases of tropical eosinophilia which seemed to be identical with the syndrome here described. KEITH, Rochester, Minn.

LIPID RETICULOENDOTHELIOSIS. A. BAEZA GOÑI and J. ESPINOZA SOTO, Rev. chilena de pediat. **15**:437 (June) 1944.

The authors report the case of a 38 month old boy with generalized lymphadenopathy, followed in three months by diabetes insipidus. Hepatosplenomegaly was absent throughout the course of the disease, which terminated fatally in two years. Roentgenographic studies revealed two areas of rarefaction in the right parietal bone. Levels of cholesterol were low in the blood but high in a biopsy specimen of lymphoid tissue.

Pathologic study resulted in a diagnosis of atypical Hand-Schüller-Christian disease: diffuse and generalized lipid reticuloendotheliosis affecting the lymphatic nodes, the posterior and intermediary lobes of the pituitary and the marrow of the ribs and the femurs. The authors stress the diagnostic significance of high cholesterol levels in lymphoid tissue.

PLATOU, New Orleans.

Diseases of Nose, Throat and Ear

LATENT TUBERCULOSIS OF THE TONSILS. G. L. COTE, Union méd. du Canada **72**:16 (Jan.) 1943.

Tonsils from 60 patients, from 4 to 27 years of age, were examined histologically. Six patients were over 20, 14 were between 10 and 15, and 40 were from 4 to 10 years of age.

Roentgenograms of the chest and gastric lavage, with search for the tubercle bacillus, had been performed on all patients. A tuberculous process was present in 8 patients (13.3 per cent). Two of these 8 patients were over 20 years of age; 6 had cervical adenopathy.

The author considers that the operation carries no risk and removes a focus (which is probably primary). He advocates routine examination of all removed tonsils to rule out latent, unsuspected tuberculosis.

DAFFINEE, Melrose, Mass.

THE RECOGNITION AND PALLIATIVE TREATMENT OF EARLY SINUS TROUBLE IN CHILDREN. H. G. BEDFORD RUSSELL, Proc. Roy. Soc. Med. **36**:401 (June) 1944.

Sinus trouble is common in children, in whom the exanthems pave the way for streptococcic infection. Tissue response to streptococci is production of edema, not pus. Insistence on the presence of pus for the diagnosis of sinusitis has occasioned nonrecognition of numerous cases in which irritation of the fifth nerve and local absorption along the lymphatics produce symptoms (e. g., "neuralgia") customarily regarded as primary in parts remote from the sinuses. Tonsillar inflammation, otitis media, conjunctivitis and headache are usually the result of sinusitis. The most cogent result of acute inflammation of the linings of the sinuses and of the nasal passages is the mechanical difficulty occasioned at the ostiums by swellings of the membrane in an inexpansible bony ring, which leads to "sinus block." The indication, therefore, is to reduce the edema at the ostiums so as to permit the normal entry of air into the sinuses and to facilitate the escape of the increased secretion. This can be achieved by the introduction of nontoxic, volatile vasoconstrictors, such as desoxyephedrine or amphetamine sulfate.

The principle of the displacement method is described.

Iodized poppyseed oil is valuable in roentgenologic diagnosis.

WILLIAMSON, New Orleans.

THE DIAGNOSIS AND TREATMENT OF SINUSITIS CHILDREN. S. E. BIRDSALL, Proc. Roy. Soc. **36**:403 (June) 1944.

In 1939 the author recorded the clinical features 80 cases of indisputable sinusitis. The cases were selected because the diagnosis had been proved beyond all doubt. It is rare that sinusitis of children is discernible by the ordinary methods of examination if properly performed. In only 13 of the 80 cases there good evidence of an antecedent cause. Of specific disease, whooping cough was undoubtedly commonest cause.

The symptoms of sinusitis are often ascribed to infection of the tonsils and adenoids.

In the series of 80 cases the most common symptoms, in order of frequency, were: (*a*) nasal obstruction, (*b*) cough, (*c*) colds, (*d*) anorexia and otorrhea.

The diagnosis was made by examination.

In conclusion, the author discusses his treatment.

WILLIAMSON, New Orleans.

FOREIGN BODIES IN THE RESPIRATORY TRACT ESOPHAGUS. R. TAPIA ACUÑA, Rev. mex. de ped. **13**:36 (Jan.-March) 1944.

The accepted principles in the diagnosis and removal of such bodies are discussed. No personal cases reported.

ABALLI, Habana, Cuba

Diseases of Lungs, Pleura and Mediastinum

STAPHYLOCOCCUS EMPYEMA IN INFANTS AND CHILDREN A REVIEW OF TWENTY-NINE CASES. CONRAD RILEY, J. Pediat. **24**:577 (May) 1944.

Experience with 29 cases of acute empyema of thorax due to Staphylococcus aureus occurring in past twenty-one years at Babies Hospital, New York is reviewed and compared with the observations reported in the literature. It is shown that whereas the incidence of empyema due to all causes has decreased since the introduction of sulfonamide therapy, the frequency of empyema due to Staph. aureus has remained almost constant, so that the relative incidence of the latter form has increased from 7.3 per cent prior to 1937 to 20.4 per cent subsequent to that date. The disease occurred most frequently in infancy, 76 per cent of the patients being under 1 year of age, with the greatest number of these less than 3 months old. There was no striking seasonal incidence. In about 80 per cent of the cases the empyema was preceded by clinical pneumonia, and in only 1 case could the condition conceivably have been interpreted as "primary empyema."

All forms of medical therapy proved ineffective, and surgical intervention appeared to be the only reasonable approach. In 4 cases recovery occurred with aspiration by needle alone; in 5, with intercostal drainage, and in 10, with rib resection. The choice of procedure was determined individually on the basis of the progress being made with conservative treatment. The length of hospitalization could not be correlated with the type of treatment. Complications attributable to therapeutic efforts were not serious; abscess at the site of insertion of the needle occurred in 6 cases, and osteomyelitis of the rib followed resection in 2 cases. The gross mortality rate for this series was 34.5 per cent, which is in fair agreement with the rate of 31.9 per cent for the 113 cases reported in the literature. Widespread pneumonia or overwhelming infection appeared to be

ses of death, and in no case could death be attrib-
d directly to the empyema.

RILEY, MC-V(S), U.S.N.R.

REVALUATION OF THE PNEUMONIAS OF INFANCY. JOHN M. ADAMS, J. Pediat. **25**:369 (Nov.) 1944.

Facts recently established as to the pathogenesis of umonia are applied to the period of infancy. Empha-is placed on the importance of aspiration or gravita- of bacteria-laden exudate into the lungs rather than inhalation of bacteria-containing droplets. Additional tributory factors include anatomic and physiologic aturity of the infant's lungs; lack of neonatal im-ity; deficiency of vitamin A as seen in fibrocystic ase of the pancreas, and conditions associated with th, such as asphyxia. The last condition greatly in-ases the incidence of congenital aspiration pneumonia.

Air-borne infections, such as the common cold and demic influenza, are predisposing illnesses, which atly increase the activity of the potential pathogens quently resident in the upper part of the respiratory ct. This conception of the dual or multiple causation he pneumonias of infancy is supported by an increas-amount of evidence that air-borne agents plus teria-laden exudates play a combined role in the elopment of pneumonia.

An unusual epidemic of "thrush" pneumonia is de-ibed, in which Monilia albicans and a strain of phylococcus appeared to have a possible synergistic on in producing the disease. The epidemic affected nfants, all of whom showed signs of pneumonia with haracteristic pattern of symptoms. One child died; ltiple staphylococcic abscesses were found on autopsy. albicans was cultured from the tongues, cheeks and ates of all 8 infants.

An etiologic classification of the pneumonias of in-cy follows:

I. Primary bacterial pneumonia
   Pneumococcic, staphylococcic, etc.; tuberculous (first infection type)
II. Primary spirochetal pneumonia
   Syphilitic (pneumonia alba)
III. Primary virus pneumonia
   Primary virus pneumonitis; psittacosis
IV. Primary mycotic pneumonia
   Thrush, blastomycosis, etc.
V. Synergistic or secondary (virus and bacterial) pneumonia. (Primary diseases include influenza [virus], measles, pertussis and the common cold)
VI. Secondary virus pneumonia (Goodpasture)
   (Primary diseases include measles, pertussis and possibly others)
VII. Aspiration pneumonia
   Congenital, amniotic, lipid, etc.
VIII. Avitaminosis pneumonia
   Vitamin A deficiency associated with chronic fibrocystic disease
IX. Eosinophilic pneumonia
   (Löffler's syndrome)

There are specific histologic changes in most of the umonias of infancy. Attention is directed particu-y to the cytoplasmic inclusion bodies seen in the helial cells, bronchial, bronchiolar and alveolar tissue patients with primary virus pneumonia and to the nonuclear exudate characteristic of this type of in-ion.

Recognition of the many etiologic factors in the pneumonias of infancy is significant for their prevention or management. So far as the prone position helps to prevent gravitation or aspiration of bacteria-laden exudate into the lungs, compensating for the immature development of the mechanisms of elimination, such as coughing and ciliary action, it may be regarded as a means of preventing pneumonia in infants. By habitual use of this position the hazard of "sudden death" or "crib death" of pneumonic origin would probably be eliminated. The strict isolation of patients with predisposing illnesses is another factor to be taken into account, in order to prevent further infection by pathogenic bacteria. The prone position offers an effective means of preventing or treating the type of cough which is related to obstructing exudate in the upper respiratory passages.

FROM THE AUTHOR'S SUMMARY.

ACCIDENTAL MECHANICAL SUFFOCATION IN INFANTS. HAROLD ABRAMSON, J. Pediat. **25**:404 (Nov.) 1944.

This study of accidental mechanical suffocation in infants under 1 year of age discloses the following circumstances underlying death:

The preponderance of deaths by smothering (85 per cent) occurred in infants under 6 months of age, with the median age at death between 2 and 3 months.

Boy babies showed a greater frequency of deaths (69 per cent) than girl babies (31 per cent)).

The peak of fatalities was reached during the late fall and early winter months, November through January.

Death from smothering took place most often between 3 a. m. and 9 a. m. There was a sharp rise between 3 a. m. and 6 a. m. in the number of deaths from smothering. This fact is significant in view of the 2 a. m. and 6 a. m. feeding times which are usual for young infants.

During the morning hours 35 per cent of the accidents occurred in cribs and 15 per cent in the mothers' beds. In the afternoon and at night baby carriages and cribs were almost equally frequent sites of accident.

In order of frequency the following were the smothering agents: (1) in the crib: blankets or outer coverings, mattresses, pillows, mattress coverings (sheets, pads and rubber sheetings); (2) in the carriage: pillows, blankets or outer coverings, mattresses and mattress coverings; (3) in the parent's bed: the mother's breast or upper extremity.

The posture most frequently noted on discovery of the infant's body was the "face down," or prone, posture (68 per cent). Fifty-five per cent of the infants suffocated in this posture were less than 5 months of age.

In only 17 per cent of the fatal cases was the body found in the "face up" posture. Almost all the infants suffocated in this posture were 5 months of age or younger. In 46 per cent of the babies found in the "face down" posture a single agent (pillow, mattress or mattress covering) was in occluding contact with the nose and the mouth, while in 22 per cent an added agent (pillow or blanket) covered the head.

In the "face up" posture pillows and blankets were found covering the face.

Deaths from overlying comprised 15 per cent of the fatalities from smothering and involved infants from 2 weeks to 3 months of age. These accidental deaths occurred most frequently during the early morning.

Attention is called to the excessive number of infants under 1 year of age who die from accidental mechanical suffocation. The number of these fatalities has in-

creased each year, until accidental mechanical smothering now holds the dubious distinction of being the leading cause of accidental death in early infancy. Yet astonishingly little concern has been evinced with regard to the problem by public health workers, and the literature contains but few comments. Concerted efforts should be made to study the problem completely, and a constructive program should be designed and disseminated to prevent deaths from accidental mechanical suffocation.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF BRONCHOPNEUMONIA. F. MORA PEREZ, Rev. mex. de pediat. **13**:361 (Oct.-Dec.) 1943.

The results of treatment in 131 infants and children with bronchopneumonia are briefly discussed. Eighty-three patients were given sulfapyridine and 48 sulfadiazine. The mortality in the first group was 8.04 per cent, and that in the second, 6.25 per cent. The fall of temperature and the duration of illness were similar in the two groups. Otitis media was the most frequent complication, developing in 14 per cent of the patients. Toxic symptoms were mild and of short duration with either drug. Vomiting was present in 25 per cent of the patients treated with sulfapyridine, as compared with 5 per cent of those who were given sulfadiazine. Only 1 patient, who received sulfadiazine, had hematuria, which was associated with crystalluria. It was controlled by increasing the fluid intake, without discontinuing the drug. In another child, treated with sulfapyridine, there developed severe leukopenia which subsided rapidly when the medication was stopped.

The plan of treatment in both groups consisted in giving 0.1 Gm. of the drug per kilogram of body weight per day. One-half this amount was administered at the start, and thereafter the daily dose was divided into six doses, given every four hours.

Treatment was continued for three or four days after the temperature had become normal and other clinical manifestations had been controlled.

ABALLI, Habana, Cuba.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

DISORDERS OF THE DIGESTIVE SYSTEM LEADING TO VITAMIN DEFICIENCY STATES IN INFANTS AND CHILDREN. RUSTIN MCINTOSH, Bull. New York Acad. Med. **20**:25 (Jan.) 1944.

In spite of adequate intake of accessory food factors, vitamin deficiency may develop as a result of faulty absorption from the gastrointestinal tract or as a result of faulty assimilation in the tissues. The situation, in the author's opinion, is not generally appreciated in spite of ample evidence of its existence. Vitamin A deficiency may be associated with pancreatic fibrosis or with prothrombin deficiency secondary to acquired hepatic disease. Deficiencies in vitamins A and K are seen in association with conditions in which there is defective absorption of food fat attributable to impairment of production and excretion of bile, and with conditions which lead to inadequate delivery of pancreatic enzymes into the lumen of the intestine, thus interfering with absorption of fat and the utilization of lipids. The vitamin deficiencies develop insidiously and are often unrecognized before an attempt at repair of damage is too late. Any suspicion of digestive disturbance in early life calls for every available clinical and laboratory procedure to detect the process, and the possibility of a developing vitamin deficiency must be kept in mind.

The water-soluble vitamins are usually readily sorbed except in severe grades of digestive disor but their proper utilization in enzyme reactions metabolic processes cannot be taken for granted. severe diarrhea there is a negative balance with re to thiamine and ascorbic acid. The forcing of f parenterally to compensate for loss of water diarrhea is not without risk of depleting the syste this group of vitamins.

JAHR, Omah

FIBROSIS OF THE PANCREAS IN INFANTS AND CHIL C. D. MAY, Proc. Roy. Soc. Med. **37**:311 (M 1944.

Almost all the exocrine portion of the pancrea involved in fibrosis. The islets of Langerhans are affected. Damage to the acini is so severe and w spread that normal production of enzymes by the g is inconceivable. This disease was present in 1 per cent of cases studied at autopsy. After having 60 patients who had this lesion in the pancreas, author became reasonably accurate in diagnosing condition during the patient's life and was able to vide suggestions for treatment. He divides pat into four groups on the basis of clinical symptoms: those dying in the first few days of life, usually as result of intestinal obstruction; (2) patients in w gastrointestinal or respiratory symptoms develop group comprises the majority of patients with lesion); (3) patients who have symptoms simila those seen in celiac disease except that pulmo symptoms may be present too (these symptoms ap only if the disease lasts a considerable time); (4) tients who live from two to four years without disorder attracting attention (a rare occurrence). child with this lesion in the pancreas has been repo to have lived longer than fifteen years. The lesion be familial. The consequences and diagnosis of lesion are also discussed in the paper.

The treatment recommended by the author is to a the patient an abundance of all types of food, regar of the appearance of the stool, for the appetite beco enormous. Use of preparation of pancreatin is diff because the doses required are so large and bec the enzyme is destroyed by the acid of the stom Predigested foods offer great promise for treat during infancy and early childhood. The vitamins be given by mouth, but doses should be four time large as usual.

WILLIAMSON, New Orlea

SHORT ESOPHAGUS IN INFANTS. M. LELONG, P. A and A. AUBIN, Presse méd. **49**:106 (Jan. 28)

Short esophagus is to be distinguished from phragmatic hernia, esophageal diverticulosis or ul tion and bilocular stomach. An infant (particular first-born male child) who vomits or regurgitates mediately after feedings and who vomits bloody m should be carefully studied fluoroscopically. Swallo of an opaque substance reveals the short esophagus the cardia above the diaphragm. (With diaphragm hernia the cardia is below the diaphragm or lies a a redoubled esophagus.) Treatment consists of thic ing the formula and maintaining the vertical pos during and immediately after feeding. The prognos not bad unless malnutrition or complications, suc spasm, ulceration or esophagitis, supervene.

DAFFINEE, Melrose, Ma

PERTROPIC PYLORIC STENOSIS IN AN INFANT. L. VELASCO BLANCO, Arch. am. de med. **18**:28 (April) 1942.

A case of pyloric stenosis in an 80 day old infant is sented. The precarious condition of the infant made author consider operation too dangerous, and he ituted a treatment consisting of duodenal tube feed- use of antispasmotics, vitamin therapy and rectal inistration of fluids. In "duodenal tube feeding" it only necessary that the catheter reach the pyloric rum; the pressure imparted to the fluid by the syringe ften sufficient to force the food through the narrowed rus.

The result obtained in the present case was satisfac- although improvement of symptoms and gain in ght occurred very slowly.

ABALLI, Habana, Cuba.

Nervous Diseases

E CLINICAL AND PHYSIOLOGICAL SIGNIFICANCE OF MAYER'S PHALANGEAL REFLEX. L. HALPERN, J. Nerv. & Ment. Dis. **99**:264 (March) 1944.

The reflex consists of maximal passive flexion of second or third finger in its basal joint. Normally, ntaneous extension and adduction of the thumb can een. In the majority of normal persons the reflex be elicited bilaterally. An exaggerated reflex on side, or, more particularly, unilateral absence of reflex, constitutes a pathologic symptom. Contra- al increase of the reflex, which then can be elicited flexion of the fourth or fifth finger too, has been rved in cases of tumor of the frontal lobe.

ases are presented for evaluation of this sign. In discussion the author concludes that Mayer's phalan- l reflex is a tone sign, absence of which is associated all organic diseases characterized by hypotonia; that its intensification is evidence of an increased tional tendency of muscle tone. It is neither a cor- l reflex nor a symptom pathognomonic of lesions of pyramidal tract.

JAHR, Omaha.

GRESSIVE LENTICULAR DEGENERATION. OLGA BRIDG- MAN and FRANCIS S. SMYTH, J. Nerv. & Ment. Dis. **99**:534 (May) 1944.

Two cases of lenticular degeneration are presented, in which an autopsy was done. The first case is that a 13 year old girl who lived approximately three rs from the time of onset of her symptoms. The dition in this case bears a striking resemblance to son's disease, with asymptomatic cirrhosis of the r. She showed evidence of progressive degeneration he lenticular nucleus.

The second case is that of an 11 year old girl with istory of hepatic disease of several years' duration ciated with splenomegaly. She showed temporary rovement after splenectomy. Two years later slur- speech developed, and she complained of difficulty novement of the voluntary muscles. Within a few ks after her admission to a hospital tremor and dity, dysarthria and dysphagia developed. A diag- s of hepatic cirrhosis was made at the time of nectomy.

JAHR, Omaha.

NINGITIS IN CHILDREN. CHARLES H. HOLLIS and AMES M. BATY, New England J. Med. **230**:278 (March 9) 1944.

Twenty-eight consecutive cases of meningitis are re- ed, and the treatment is described. In cases of influenzal and pneumococcic meningitis the combination of specific antiserum and sulfonamide compounds was used; this appears to be the most effective therapy. With meningococcic meningitis, sulfonamide therapy alone was used; this is apparently sufficient to effect a complete cure, except in cases of fulminating meningococcic septicemia.

The mortality in this series was as follows: 2 of the 9 patients with influenzal meningitis; 2 of the 12 patients with meningococcic infection, both of whom were infants with acute meningococcemia and the Waterhouse-Friderichsen syndrome, and 4 of the 5 patients with pneumococcic meningitis, all under 8 months of age. Of the others, 1 with meningitis due to the colon bacillus survived and blindness developed as a sequela, and 1 died of meningitis due to Salmonella Orienienburg.

AUTHORS' SUMMARY.
GENGENBACH, Denver.

MENINGITIS DUE TO SALMONELLA ORANIENBURG. CHARLES H. HOLLIS and ELMER W. BARRON, J. Pediat. **24**:568 (May) 1944.

A fatal case of meningitis due to *Salmonella oranienburg* in an infant is reported, together with the important autopsy data. The literature on Salmonella meningitis is reviewed briefly. The results suggest that treatment with the sulfonamide compounds is effective for certain types of Salmonella meningitis. The best results have been obtained with sulfapyridine (3 cures) and with sulfanilamide (1 cure).

FROM THE AUTHORS' SUMMARY.

MENINGITIS DUE TO PITTMAN AND NON-PITTMAN STRAINS OF H. INFLUENZAE. J. GORDON, HESTER WOODCOCK and K. ZINNEMANN, Brit. M. J. **1**:779 (June 10) 1944.

Few cases of influenzal meningitis have been classified serologically in Britain, and only recently has any one tried to determine the group of the influenzal organism present. The authors report on 2 patients with the non-Pittman type of meningitis who were treated with sulfapyridine, with recovery. In both cases the organisms had a rough appearance on culture and did not type with the specific serum. The authors report on 3 other patients who had type B influenzal meningitis, 2 of whom died and 1 recovered after a rather long illness. These patients were treated with sulfathiazole and sulfapyridine. No serum was used. The authors state that it is generally thought that the non-Pittman strains are nonpathogenic and cite their 2 cases of mild meningitis as evidence that they are pathogenic for man. In their summary, they state that it is advisable to type the organism in all cases of influenzal meningitis to determine any possible difference in prognosis and treatment.

BIRDSONG, University, Va.

SPONTANEOUS VENTRICULAR RUPTURE IN HYDROCEPHALUS WITH SUBTENTORIAL CYST FORMATION. J. PENNYBACKER and D. S. RUSSELL, J. Neurol. & Psychiat. **6**:38 (Jan.-April) 1943.

Pennybacker and Russell report 2 cases of hydrocephalus resulting from obstruction of the aqueduct in which the dilatation of the lateral ventricles was accompanied by rupture of their walls in the region of the vestibule, producing a subtentorial cyst which communicated with the lateral ventricle. The site of rupture was that part of the ventricle wall which is thinnest normally, i. e., in the medial angle of the

collateral trigone, between the forward-sweeping crus of the fornix and the forceps major. In a third case of hydrocephalus resulting from occlusion of the foramens in the fourth ventricle, by adhesive arachnoiditis thinning occurred without rupture of this area of the wall of the lateral ventricle. Ventriculographic examination established the diagnosis. The treatment advocated by the authors is, first, the establishment of an opening in the anterior part of the third ventricle and, if this proves ineffective, a collapse of the cyst by the cerebellar approach.

MALAMUD, Ann Arbor, Mich.
[ARCH. NEUROL. & PSYCHIAT.]

MENINGITIS DUE TO PFEIFFER'S BACILLUS. RAMIRO VALLEDOR, Bol. Soc. cubana de pediat. **16**:58 (Feb.) 1944.

This is a report of 7 cases of meningitis due to Hemophilus influenzae, with recovery in 2 instances. One of the 2 patients who recovered received sulfadiazine alone. The other received sulfadiazine, sulfapyradine and 50 mg. of rabbit serum (Alexander). The 5 patients who died received sulfanilamide, sulfapyradine in maximum doses, complement and transfusions. The author considers combined sulfadiazine and serum therapy the ideal treatment for this disease.

KEITH, Rochester, Minn.

CYCLOCEPHALON AND HYPERTROPHIED STRUCTURES IN THE BRAIN OF A CHILD WITH MULTIPLE FACIAL MALFORMATIONS. JULIO ARANOVICH, Rev. neurol. de Buenos Aires **8**:312 (July-Sept.) 1943.

A male child died on the seventh day of life, with hyperthermia. Except for congestion of the liver, spleen and lungs, autopsy revealed nothing abnormal in the internal organs. Microcephaly, microphthalmia on the left side and multiple chondromas of the face were present.

Macroscopic examination of the brain showed pronounced malformation of both cerebral hemispheres. They formed a large single vesicular structure with absence of fissuration and depressions on the lateral surfaces in the region of the sylvian fissure. There was slight indentation at the anterior extremity of this vesicle, at the site of the interhemispheric fissure.

At the base there was typical arhinencephaly, with absence of the olfactory bulbs, nerves and tracts; there was only one ventricle and no corpus callosum; a diverticulum from the roof of the third ventricle pushed the anterior part of the vermis posteriorly; the pyramidal tracts were entirely absent; the anterior part of the vermis and the dorsal nuclei of the thalamus were poorly developed; there was complete absence of the optic radiations and olfactory pathways; the cerebral cortex was arrested in development, the stage corresponding to that usually seen in the second month of fetal life; there was complete absence of association, commissural or projection fibers in the cerebral cortex; the region of the cornu ammonis was the most normally developed part of the brain on either side, and the olives, red nuclei and hypothalamic region were hypertrophied.

The author believes that arrest of development of the neoencephalon permitted inordinate growth of paleoencephalic structures. He postulates a disturbance in circulation of the cerebrospinal fluid in the first to the third month of fetal life to account for the bulge in the roof of the third ventricle and the arrested development of the cerebral cortex.

SAVITSKY, New York.
[ARCH. NEUROL. & PSYCHIAT.]

Psychology and Psychiatry

PERSONALITY FACTORS IN A MOTOR SPEECH D... CASE. CATHINKA MARIE RUSSELL, Am. J. M... Deficiency **49**:171, 1944.

A boy aged 5 years did not talk. He had ... variously recorded as imbecile to bright and intelli... Motor function of the tongue and motor control of sp... were poor; he had facial and bodily tics, and his ... tude was one of extreme negativism. Hearing ... normal; the stature normal, and there was no ... organic defect. His one response was "ngah," and ... a long time every new sound was prefaced with ... response. When he began to learn, he had del... responses, backward speech and stuttering. He fi... recovered speech, had a good school record and i... present attending college. The author states that ... with this case calls further attention to the vast am... of research and experimentation necessary on cer... types of children who do not appear to have nor... intelligence or any possibility of attaining social m... rity.

PALMER, Wichita, Ka...

AN UNUSUAL FAMILAL SYNDROME. A. P. FRIED... and J. E. ROY, J. Nerv. & Ment. Dis. **99**:42 (J... 1944.

This paper deals with a report on 6 feeblemi... children in one family, all of whom showed iden... defects in the nervous system. The outstanding cli... features were feeblemindedness, strabismus, exte... plantar reflexes and bony deformities of the feet.

The father had a high average intelligence; ... mother's intelligence quotient was normal. A mate... aunt had convulsions and was said to be mentally ... fective. The parents of the 6 children were cousi...

The electroencephalogram of the mother and t... of the 6 siblings showed a striking similarity, wi... uniform tendency to high voltage and irregular ... quencies. The electroencephalogram of the father ... not remarkable.

JAHR, Omah...

PERSISTENCE AND CHANGE IN PERSONALITY PATT... KATHERINE ELLIOTT ROBERTS and VIRGINIA ... DYNE FLEMING, Monograph of Society for Rese... in Child Development, 1943, vol. 8, no. 3.

This monograph on personality development is ... second study published by the Merrill-Palmer scho... the result of several years of research in the advi... service for college women. The first publicatio... "Women After College," by Robert G. Foster ... Pauline P. Wilson. This second study, based o... tensive life histories of 25 college women typica... and selected from a larger group of 100 cases, atte... to answer some questions about the persistence ... fluctuation of traits and attitudes. Some of these ... tions are: Does the childhood personality pattern pe... into adulthood relatively unchanged, or is the... notable variation? What are some of the factors w... influence personality development? What is the e... on personality development of a happy home du... childhood? Is there any difference in the person... patterns of happily and of unhappily married women...

A detailed analysis is made of the histories, ... results are given in charts and tables. Three cases ... presented in descriptive form to illustrate the dev... ment from childhood to adulthood and to show som... the factors which influence development. In every ... son a nucleus of traits persisted from childhoo...

lthood while some traits fluctuated. But there was e persistence than change. Both case studies and stical analysis show that personality is related to kind of relationships existing in the home. The ber of cases analyzed is small, but the trend of the lts indicates that those women who are happily ried show more wholesome personalities than those are unhappily married. Implications for education discussed.

FROM THE AUTHORS' ABSTRACT.

BITS IN INFANCY AND THEIR INFLUENCE ON THE CHILD'S PSYCHE. V. SANTAMARINA, Arch. de med. nf. **11**:28 (Jan.-March) 1942.

he author proposes a national campaign for educa- in the mental hygiene of infancy, to be sponsored the Cuban Pediatric Society. He discusses habit ation from birth to puberty, showing the commonest rs in education of children.

BRIBIESCA, Zamora, Mich., Mexico.

ABLISHMENTS FOR MENTALLY ABNORMAL CHILDREN. osé PEDRO ACHARD, Bol. Inst. internac. am. de otec. a la infancis **18**:92 (March) 1944.

he author considers that although in Uruguay there already various establishments for mentally abnor- children, it is still necessary to organize separate itutes for the special treatment of certain kinds of rmal children; also, some of the institutes already ting need guidance to make the reeducational work they carry more efficient.

EDITOR'S SUMMARY.

STERICAL COMA IN A GIRL OF 8 YEARS. ROBERTO FRAGA ARROYO, Bol. Soc. cubana de pediat. **16**:43 (Feb.) 1944.

rare case of coma due to hysteria is presented. irl of 8 years had generalized muscular rigidity and ractures, nystagmus and blepharospasm and re- ded to none of the usual stimuli. All laboratory minations, including studies of the spinal fluid, gave nal results. The author feels that hysteria in chil- is more frequent than is realized. The patient was ted by suggestion and recovered completely after e months in bed.

KEITH, Rochester, Minn.

Diseases of the Genitourinary Tract

LAPSE OF URETHRA IN A CHILD OF 6 YEARS. J. CHASSAR MOIR, Proc. Roy. Soc. Med. **36**:436 (June) 944.

he patient, a little girl, suddenly started to bleed n the vulva. She was sent to a hospital the next There was still a slight loss of blood, and the d complained of soreness. A dark red, velvety s nearly 1 inch (2.54 cm.) in diameter bulged be- n the labia and obscured all the structures in that on. With anesthesia fuller examination was possible, it became obvious that the condition was an ex- ive prolapse of the mucous membrane of the urethra. passage into the bladder was situated at the pos- r part of the mass. With firm, sustained pressure mass was replaced, and a catheter was inserted into bladder with the hope that the constant pressure ld prevent a renewed protrusion of the mucosa. treatment was only partially successful; so later mucosa was excised. The child made an uneventful very. At no time had she any difficulty with urition.

WILLIAMSON, New Orleans.

SEMINOMA OF THE TESTES IN AN INFANT. VALDÉS DÍAZ, SÁNCHEZ SANTIAGO, DÍAZ ROUSSELOT and SALAZAR, Arch. de med. inf. **11**:23 (Jan.-March) 1942.

An 8 month old white boy had a large, lemon-sized tumor of the scrotum, of three months' development. Resection was performed, and pathologic study revealed a seminoma. After operation, irradiation of the lumbo-aortic glands was instituted but had to be discontinued because of vomiting, diarrhea and fever. Blood transfusions, venoclysis and administration of liver extract were used thereafter. The patient was discharged in good general condition.

BRIBIESCA, Zamora, Mich., Mexico.

COMPARATIVE BACTERICIDAL EFFECTS OF SULFATHIAZOLE AND ORGANIC ACIDS IN URINE INOCULATED WITH HUGE NUMBERS OF BACTERIA. HENRY F. HELMHOLZ, Bol. Soc. cubana de pediat. **15**:847 (Dec.) 1943.

This study was undertaken to compare the bactericidal action of sulfathiazole and that of mandelic acid in urine inoculated with huge numbers of bacteria, approximating a condition that one would have in the urinary passages with obstruction. With the bacterial content in millions per cubic centimeters sulfathiazole produced practically no reduction in the number of organisms, while with the bacterial content in the hundreds of thousands per cubic centimeter sulfathiazole in the same concentrations produced a definite reduction in the number of organisms. With betaoxybutyric acid, as well as with mandelic acid, no matter how large the inoculation, when the p_H of the urine and the concentration of the acid brought it into the bactericidal range, there was a definite bactericidal effect even when the number of bacteria was several millions per cubic centimeter. It seemed, therefore, in treatment of urinary infections associated with stasis that mandelic acid should be used, or if possible, the ketogenic diet, for no one has shown that betaoxybutyric acid in the concentrations excreted by the kidney produces any irritation of the kidney or urinary passages which are not free of mandelic acid.

FROM THE AUTHOR'S ABSTRACT.

Diseases of the Ductless Glands; Endocrinology

RECOVERY OF INJECTED CHORIONIC GONADOTROPIN FROM RABBIT URINE. A. A. SALMON and E. C. HAMBLEN, Endocrinology **33**:257 (Oct.) 1943.

A study was undertaken to determine what percentage of injected chorionic gonadotropin is excreted in the urine.

In rabbits the amount of gonadotropin recovered during the first ninety-six hours after administration of the substance was 5.7 per cent of the total dose injected. No gonadotropin was found in the urine after ninety-six hours.

JACOBSEN, Buffalo.

HYPERTROPHY OF THE THYMUS. D. LONGPRÉ, Union méd. du Canada **72**:901 (Aug.) 1943.

Pediatric opinion is still divided as to the meaning of thymic hypertrophy. The function of the thymus is unknown; hypertróphy may be due to hyperfunction, or perhaps to hypofunction. There is no proof of any thymicolymphatic system. Roentgenographic diagnosis of hypertrophy of the thymus is difficult, and clinical diagnosis is unreliable.

Longpré presents 6 cases in which the clinical diagnosis of thymic hypertrophy was made. In only 1 of these was the diagnosis verified at autopsy, and in this case the roentgenologic diagnosis was not definite. In 2 cases the condition was probably tetany, but diagnosis was not verified. In 2 other cases there were congenital lesions of the heart. In the remaining case the patient died of massive influenzal pneumonia.

Longpré cites Brennemann in conclusion: "It would be a safe procedure to consider the possibility of thymic pressure in all cases of asphyxia, but to realize that it is an infrequent cause of this symptom."

DAFFINEE, Melrose, Mass.

ROENTGENOGRAPHIC DIAGNOSIS AND TREATMENT OF HYPERTROPHY OF THE THYMUS. R. GRONDIN, Union méd. du Canada **72**:904 (Aug.) 1943.

The author draws attention to the difficulties of making the diagnosis of hypertrophied thymus from roentgenograms. He stresses the importance of taking the pictures with the child in the upright position and placed at a right angle to the rays. The image is more nearly perfect at the end of expiration, but not with forced expiration, such as crying.

DAFFINEE, Melrose, Mass.

REPORT ON TWO PAIRS OF BROTHERS SHOWING MARFAN'S SYNDROME. H. J. STERN, Brit. J. Ophth. **28**: 229 (May) 1944.

The oldest brother of the first pair was 14½ years of age, underweight and undeveloped; he showed hypogenitalism, an undescended right testicle and a small left testicle. There were frequent extrasystoles and prominent hypertrophied veins over the chest. The limbs and fingers were characteristic of the syndrome. There was incomplete embryotoxon. The pupils were irregular in shape, and there was iridodonesis. There were two small bridge colobomas of the iris. In its temporal lower part the iris showed a peculiar spongy structure, so that the parenchyma partly floated in the anterior chamber. Both lenses were luxated. The sella turcica was very small.

The younger brother was 12 years of age. He was undersized. Arachnodactyly was present. Both lenses were displaced.

The parents were healthy and normal. The sella turcica of the father was small.

The parents and the other children of the second pair of brothers suffered with more or less severe obesity of endocrine origin. Several members of the family had high myopia.

The older brother was 14 years of age and was oversized but well developed. Arachnodactyly was present. There was habitual subluxation of the humerus and of the fingers. The sella turcica was small. There was subluxation of both lenses.

The younger brother was 11 years of age. He was oversized and presented the same general anomalies as his brother. Both lenses were subluxated.

The author believes the 4 cases presented support the views expressed by Mann that the disturbances in Marfan's syndrome are probably only coordinated symptoms of a genotypic disturbance, producing general and ocular troubles which affect not only the mesoderm but the endocrine glands and the ectoderm.

W. ZENTMAYER. [ARCH. OPHTH.]

SYMPATHICOBLASTOMA OF THE ADRENAL GLAND IN CHILD OF 18 MONTHS. D. D. SOSA BENS, J. JIMÉ and L. BARRERAS AREU, Bol. Soc. cubana de pe **15**:509 (July) 1943.

The authors review the literature, beginning Virchow, in 1864. They report a case of sympath blastoma in an 18 month old child with metastase the face and in both femurs. The roentgenograms the photomicrographs of tumor tissue are reprodu The importance in diagnosis of smears of the blood the bone marrow is emphasized.

KEITH, Rochester, Min

PERIARTERITIS NODOSA OF KUSSMAUL AND MAIER. GALAN and M. PEREZ-STABLE, Bol. Soc. cuban pediat. **15**:635 (Oct.) 1943.

This is an extensive and careful review of the w subject of periarteritis nodosa. The authors state they are describing in another bulletin the first cas this disease in a child to be reported from Cuba. T review the literature in detail, point out the diffe etiologic theories and in many instances give tab summaries of the work reported by other authors s Kussmaul and Maier's original contribution, in 1 They discuss the pathologic anatomy, the clinical s and symptoms, the prognosis, the diagnosis and w little treatment has been recommended. They b the subject up to date, in 1943, and make this an ex lent reference article for any one interested in the de of the subject.

KEITH, Rocheste, Min

DIABETES IN CHILDHOOD. J. BONABA and M. L. SAL DE RODRÍGUEZ, Bol. Soc. cubaa de pediat. **15** (Dec.) 1943.

The authors discuss diabetes in children in consi able detail, pointing out its essential characteristic relation to such factors as evolution, prognosis treatment. They discuss complications and outline treatment with regard to diet, use of insulin, "techn social" assistance and adjuvant treatment (vit therapy, opotherapy and calcium therapy).

KEITH, Mayo Clinic, Rochester, Min

Diseases of the Muscles, Bones, Joints and Lymph Glands

CALCINOSIS UNIVERSALIS IN AN INFANT. B. SÁN SANTIAGO and R. PEREIRAS, Arch. de med. inf. (Jan.-March) 1942.

The authors review the literature on calcinosis versalis, with special reference to the etiology, present a clinical case. A 14 month old white boy a history of lumbar pain when lifted, generalized e and temperature reaching 39 C. (102.2 F.) at the ag months. On his admission to the hospital he had nu ous disseminated, hard nodules and plaques, several abscesses and pronounced generalized spasticity. R genograms revealed calcareous deposits throughout body. The blood chemistry was normal. There slight anemia, with a red cell count of 2,900,000. Bi confirmed the diagnosis of calcinosis universalis.

BRIBIESCA, Zamora, Mich., Mexi

POCHONDRODYSTROPHY: REPORT OF A TYPICAL CASE. J. ROJAS DOMINGUEZ, Rev. mex. de pediat. **13**:361 (Oct.-Dec.) 1943.

The author reports a case of lipochondrodystrophy so known as dysostosis multiplex, gargoylism and urler's syndrome) in a 6 year old child.

The patient showed characteristic somatic alterations, luding typical facies, greatly shortened neck, short nk, malformed arms and "half-crouched" posture, to generalized limitation of extension of the joints. There was an opaque, milky white ring at the upper of the corneoscleral junction but no definite corneal city. Noisy breathing due to nasal obstruction was ed. The heart was slightly enlarged, and the blood ssure was elevated (120 and 140 systolic and 90 stolic). The edge of the liver was below the costal rgin, but the spleen was not palpable. There was mental retardation. Roentgenograms of the shoulder upper extremity showed typical changes. The car- centers of ossification corresponded to those of a 2 r old child. There was moderately severe anemia. e electrocardiogram showed low complexes in leads and III, the former being indicative of myocardial nage.

confirmatory biopsy was not performed. The outding features of the illness are reviewed, and the rations of lipid metabolism are discussed.

ABALLI, Habana, Cuba.

Diseases of the Eye

LYCTENULAR CONJUNCTIVITIS. L. VELASCO and B. V. RE, Arch. am. de med. **18**:6 (Jan.) 1942.

The authors discuss the clinical aspects of the con- on and consider the various hypotheses of patho- esis which have been presented. They favor the ion that it is a manifestation of tuberculosis, related a high degree of allergy to tuberculin. They note in a series of 150 patients with phlyctenular con- ctivitis observed by them at the Fiorito Hospital the adermal tuberculin test gave a strongly positive re- on in every instance; frequently there were asso- ed clinical and roentgenographic evidences of intra- acic involvement.

ABALLI, Habana, Cuba.

TIC FORMATIONS IN THE VITREOUS BODY: A CLINICAL CASE. JOSÉ SAENZ CANALES, An. Soc. mex. de ftal. y oto-rino-laring. **17**:123 (July-Aug.) 1942.

anales refers to this anomaly as an ophthalmologic osity since it is rarely seen by the oculist, as it not alter the normal condition of the eye and the ent does not seek medical advice unless some inter- ent condition is present.

he following classification of cysts of the vitreous made: cysts located in the anterior part of the eous, near the crystalline lens; cysts located in the posterior part of the vitreous, in the vicinity of the optic disk, and cysts free in the vitreous body.

Of the first type the following subtypes are considered: cysts produced by anterior remains of the fetal hyaloid vascular system, a lesion which may or may not be associated with opacities in the crystalline lens; cysts produced by remains of the anterior portion of the canal of Cloquet, and cysts of ciliary origin, which may be congenital or acquired.

Of the second type the following subtypes are defined: cysts formed by posterior remains of the fetal hyaloid vascular system; cysts representing the posterior remains of the canal of Cloquet; cysts formed by mesodermal remains of the fetal cleft, and cysts of uveal origin, which may be congenital or acquired.

Of the third type two subtypes, congenital and acquired, are described.

Detailed descriptions of the appearance of all these cysts are given, and numerous citations from the literature are made. The differential diagnosis is well discussed.

The author reports a clinical case. A patient aged 32 complained of poor vision for distance, which was worse in the right eye. Visual acuity in the left eye was 7/10 and could be improved to 8/10 with the pinhole disk; in the right eye it was 4/10 and could not be improved. Both eyes showed opacities in the vitreous, as well as well defined, disseminated pigmentary changes in the retinas; a cystic formation was observed in the region of the papilla in the right eye. The author diagnosed the lesion as a cyst of the vitreous and classified it as a cyst formed by the posterior remains of the fetal hyaloid vascular system. The pigmentary changes he believed to be hereditary, probably syphilitic. General physical examination revealed nothing significant.

H. F. CARRASQUILLO. [ARCH. OPHTH.]

Skin Diseases; Allergy

THE USE OF STRAINED MEATS AS THE PROTEIN BASIS FOR MILK SUBSTITUTES IN THE TREATMENT OF MILK ALLERGY. JEROME GLASER, New York State J. Med. **43**:2399 (Dec. 15) 1943.

Animal meats and soybeans are the only foods other than milk that provide the infant with the necessary amino acids. Rowe, in 1931, made use of beef and lamb meat juice as milk substitutes. Glaser and Landau, in 1935, used dried, ground, fat-free beef muscle as a milk substitute in a case of eczema.

A boy aged 9 months, with severe eczema, was given a lamb meat substitute with corn oil and taro flour. Thoroughly dried meat was forced through a perforated steel plate. The finished product was a finely strained meat. This food was fed through a small catheter. Excellent results were obtained, and within eight weeks the child's skin was in perfect condition.

AIKMAN, Rochester, N. Y.

Society Transactions

SOCIETY FOR PEDIATRIC RESEARCH

JOSEPH A. JOHNSTON, M.D., *President*

Fifteenth Annual Meeting, Atlantic City, N. J., Sept. 25-26, 1944

First Session

Monday Afternoon, Sept. 25

Active Immunization of Children with Shigella Paradysenteriae and Shigella Sonnei. DR. MERLIN L. COOPER, DR. JACK TEPPER (by invitation) and MISS HELEN M. KELLER (by invitation), Cincinnati.

Separate groups of children were immunized with killed suspensions of Shigella paradysenteriae types W, X and Z and with Shigella sonnei. Blood serums obtained before immunization and at regular intervals after immunization were studied for their passive mouse-protective power. The protective power of the immune serums as compared with the protective power of serums obtained before immunization showed increases ranging from 13 to 645 fold.

Blood obtained at intervals after immunization showed a gradual decrease in protective power, but serums obtained twenty-four weeks after immunization still showed statistically significant increased protective powers against the homologous challenge cultures. Immunized groups of children have not been studied for a longer period. The average LD_{50} protective volumes of serum from the immunized children were much smaller and were more protective than the average LD_{50} protective volumes of serum from 11 children convalescing from dysentery.

The homologous and heterologous immune responses stimulated by injection of single antigens showed that the homologous immunity was always greatest, that the heterologous immune response was statistically significant for some types and not significant for others and that there was almost no cross immunity between S. sonnei and the S. paradysenteriae types. Immunization with a combined antigen containing S. paradysenteriae types V, W, Z and Boyd 88, and S. sonnei, the shigella causing the majority of cases of dysentery, stimulated a statistically significant immune response to each of the component antigens.

These results indicate that active immunization with such a combined antigen may offer protection to persons subsequently exposed to dysentery.

Renal Function in Children. MISS HELEN M. RANNEY and DR. DONOVAN J. MCCUNE, New York.

The application to children of modern methods of studying renal function by the technics of clearance and saturation has been held back by analytic difficulties involving diodrast and inulin. These obstacles have been largely removed by Smith's introduction of sodium paraaminohippurate—easily measurable by the familiar Marshall reaction—as a substitute for diodrast and by the development in our laboratory of a micromethod for inulin. The present paper is a preliminary re of interrupted studies, the first aim of which wa investigate the applicability of these methods to dren and the final end to extend the descriptio renal function to very young infants.

The ages of the subjects varied between 3 an years. In this age group we have found it feasibl determine clearances by injecting inulin subcutaneo in an approximate 25 per cent solution and, forty minutes later, injecting sodium paraaminohippurate the same site in a concentration of about 2 per Two hundred milligrams of inulin and 30 mg. of so paraaminohippurate per kilogram of body weight yield satisfactorily stable serum values of about 10 2 mg. per hundred cubic centimeters respectively approximately two hours. The method is more venient than that of continuous intravenous infu Determination of tubular excretory maximum dem a serum concentration of paraaminohippurate of 80 per hundred cubic centimeters. This concentra cannot be attained except by continuous infu Priming and sustaining solutions are prepared given as has been described by others. For pr timing of collection periods and for insurance of plete evacuation an indwelling catheter is essential bladder must be washed quantitatively at the en each period. Since the manipulations are rather consuming, it is difficult to shorten the periods b ten minutes; twenty minutes is more satisfac Samples of blood are removed at the beginnin each period.

We have had no trouble with the administratio inulin in this manner, although it must be admitted the proper purification of the crude material is ted Sodium paraaminohippurate causes mild and brief comfort when put under the skin. When it is introd by vein as a 10 per cent solution at a speed which raise the serum concentration to 80 mg., the chil often complain of feeling hot or even of being "on The nature and vividness of the complaints of the excitable subjects may really alarm the operator. trary to Smith's experience, our observation has that the subjective manifestations do not consist abate when the rate of infusion is slowed, but the disappear at once when the experiment is ended. should be emphasized that we have detected no acce tion of pulse in proportion to the degree of excite and no significant alteration of blood pressure. Sur is evidently an important element of the phenom for children who reacted violently during the first have remained completely placid throughout a se

Inasmuch as a determination in duplicate of clearances of inulin and paraaminohippuric acid an the tubular maximum of the latter uses approxim three hours of the time of an experienced operator an assistant and twelve hours of the time of a comp technician for analysis of the specimens, the examin evidently remains a research instrument and is n clinical tool. While the cooperation of the subje not essential, children will occasionally be encount who are so refractory that the test will be ende mutual consent. In view of the effect of the epineph

renal blood flow the emotional state of the subject ould be recorded.

Compared on the basis of surface area or tubular cretory mass, the values which we have obtained respond closely with those reported for adults. These dings have, of course, no bearing on what may be pected in early infancy—a period which we have not been able to explore. A few observations in cases renal disease have yielded results which will be cribed elsewhere.

timation of Renal Function in Children with Glomerulonephritis and Nephrosis. Dr. Mitchell I. Rubin, Dr. Milton Rapoport and Mrs. Molly Randall, Philadelphia.

Glomerular filtration and renal blood flow of normal ildren between the ages of 7 and 10 years and patients th acute glomerulonephritis, acute glomerulonephritis d nephrosis combined and chronic glomerulonephritis th the nephrotic syndrome were investigated, using mannitol, sodium paraaminohippurate and urea arance tests. There was a noticeable disparity tween the degree of anatomic inflammatory change sent, as indicated by the urinary sediment, and the gree of functional alteration.

The mannitol and sodium paraaminohippurate clear- ce values for the normal children were the same as se reported for adults. While the urea clearance lues above the augmentation limit of 2 cc. per minute ried directly with the flow of urine, the changes in w did not affect the mannitol clearance values.

In the early stages of acute glomerulonephritis there s a sharp reduction in the mannitol clearance and urea clearance. In a child with a twenty-four hour ine volume of 100 cc. glomerular filtration was re- ced to about 4 per cent of normal, a fact which ggests that oliguria in acute glomerulonephritis is rgely dependent on deficient glomerular filtration. crease in these clearance values occasionally persisted some time after the anatomic inflammatory lesion d shown almost complete healing. The sodium para- inohippurate clearance returned to normal more ickly than did the mannitol clearance.

When acute glomerular disease coexisted with acute phrosis, the decrease in the mannitol clearance was striking contrast to the high mannitol clearance seen th pure nephrosis.

In the patients with chronic glomerulonephritis with without the nephrotic syndrome there were decreases mannitol and urea clearances. Despite the reduction the glomerular filtration rate, some of these patients d a good urinary flow, suggesting the existence of a fuction in the tubular capacity to reabsorb water. ore extensive studies are in progress on patients with rious renal diseases; these studies will form the basis a future report.

osporus Clearance in Children with Vitamin D–Resistant Rickets. Dr. Howard W. Robinson and Dr. Waldo E. Nelson, Philadelphia.

A study of the phosphorus clearance was made on children between the ages of 3 and 14 years whose chitic condition was helped only by massive doses ntaining 50,000 to 400,000 U. S. P. units daily) of a paration of vitamin D during approximately one and -half years. Phosphorus, inulin and diodrast clear- ce values were obtained during the active and the aled stages of the disease. On two occasions during year studies of the calcium and phosphorus balances re also made on 4 of the children during active and healed stages of rickets, three day tests being employed. In all instances the children showed slight positive calcium and phosphorus balances. After vitamin D was administered, the serum inorganic phosphorus was always increased. However, the values for the phosphorus clearance were not changed by this increase in serum phosphorus, nor did these values differ from those of children with no renal disorders. Thus, phosphorus clearance values did not differ greatly even when the level of serum inorganic phosphorus varied from 1.6 to 5 mg. per hundred cubic centimeters. Judging from an estimate of glomerular filtration obtained from the inulin clearance, it was calculated that between 75 and 95 per cent of filtered inorganic phosphorus was reabsorbed by the renal tubules. Evidence was obtained from 2 of the patients indicating that the rate of glomerular filtration was decreased by large doses of vitamin D, which were effective in raising the serum levels of inorganic phosphorus.

A Congenital Defect of Water Metabolism. Dr. Antonio J. Waring, Savannah, Ga.; Dr. Laslo Kajdi, Baltimore, and Dr. Vivian Tappan, Tucson, Ariz.

A group of 6 cases were presented which showed a syndrome involving the renal mechanism for water resorption. The patients in 3 of the cases were half-brothers. Two cases were studied at the Children's Hospital, Boston, and 4 at the Johns Hopkins Hospital, Baltimore. Similar cases have been described under the loose diagnosis of "diabetes insipidus," but we feel that the syndrome is distinct enough to warrant separation of these cases as a group.

The syndrome is characterized by (1) onset shortly after birth, (2) erratic and unexplained fever, (3) persistent constipation, (4) vomiting (during the first three months of life), (5) polydypsia and polyuria, which do not respond to pitressin, (6) high values for serum sodium and chloride, (7) high skin resistances, (8) rapid dehydration if fluids are reduced or withheld, (9) inability to excrete urine of a high specific gravity, (10) familial incidence and (11) occurrence in boys only (?).

The presenting complaints were unexplained fever, failure to gain weight and constipation. Examination resulted in the findings just enumerated. The level of serum sodium sometimes reached 170 to 180 milliequivalents per liter and that of chloride 120 to 140 milliequivalents. The bouts of dehydration are usually not associated with acidosis.

The thirst of 1 of the patients studied was satisfied only when five to six times the normal requirement of fluid was offered. The levels of serum sodium and chloride decreased to normal, and the infant remained afebrile on this high fluid intake. When the fluid intake was restricted to about half of that desired by the patient, his temperature rose, and the levels of serum sodium and chloride became pathologically high. With total restriction of fluids the infant became severely dehydrated within twelve hours; the flow of urine virtually ceased in ten hours; the temperature rose, and the serum sodium and chloride increased greatly, while the protein, the nonprotein nitrogen and the hematocrit readings remained normal or only slightly elevated unless the dehydration was further prolonged. The dehydration could be corrected rapidly by giving water. The partition of chloride between the plasma and the blood cells was normal with both normal and elevated levels of chloride. When 2 Gm. of sodium chloride was added to his standard feeding formula and free intake of fluids allowed, the infant gained weight, began to sweat

and had normal skin resistance for the first time the levels of serum sodium and chloride remained normal. The urinary excretion of sodium and chloride rose but did not account for the total intake of sodium chloride.

Pitressin was given until toxic reactions were seen without any alteration in fluid intake or output. The urinary excretion of sodium increased, however.

Renal clearances done under good conditions of hydration showed normal values for mannitol, urea, phosphates and paraaminohippuric acid at high and low levels. When the fluid intake was reduced, however, renal function as reflected by these clearances became progressively impaired. It was found that only 70 to 80 per cent of the filtered water, as against 99.5 per cent of the filtered sodium and 98.8 per cent of the chloride, was reabsorbed in the renal tubules. Administration of ammonium chloride per os revealed that the children could excrete acid urine.

Results of dextrose and dextrose-insulin tolerance tests and 17-keto steroid excretion were normal, as was development of the bones and sexual development.

In 1 child, who died, autopsy showed normal adrenals and mildly hydronephrotic kidneys.

These studies indicate that the patients had a specific defect in tubular resorption of water. Some similarity exists to the conditions produced by pituitary-hypothalamic lesion, by repeated administration of desoxycorticosterone acetate and by intoxication with the sulfonamide compounds (Luetcher).

Relation of the Lymphocyte to Local Formation of Antibodies. Dr. T. N. Harris and Dr. W. E. Ehrich, Philadelphia.

The cells which form antibodies have never been identified, although the prevalent opinion has been that reticuloendothelial cells are involved. Masta and Hudack, however, found antibodies in the extract of the regional lymph node after injection of an antigen into the ear of the rabbit.

The object of this work was to analyze the role of the lymphatic system in the formation of antibodies. The pad of the hindfoot of the rabbit was selected for the injection of an antigen, because it has only one regional lymph node, the popliteal; therefore, it was thought that a study of that node and its associated lymph vessels might permit a complete description of the local reaction of the lymphatic system to injection of the antigen. It was found that antibodies could not be demonstrated in extracts of the tissue at the site of injection or in the afferent lymph to the popliteal lymph node but that in extracts of the regional lymph node and in the efferent lymph antibodies appeared at approximately the third day after the injection and rose in titer until the sixth or seventh day. In the course of that period the titer of the efferent lymph was not infrequently found to be higher than that of the blood serum at the same time.

During the period of the rise of antibody titer in the efferent lymph there appeared a sharp rise in the size of the lymph node, caused by a diffuse lymphatic hyperplasia, which was followed by development of germinal centers and a sharp increase in the output of lymphocytes into the efferent lymph.

When the lymphocytes were separated from the supernatant lymph, it was found that the antibody titer of the contents of the cells was substantially higher than that of the surrounding fluid. This difference was greatest at the time of the greatest rate of increase of antibody titer in whole lymph.

Incubation of lymphocytes containing one species antibodies with lymph supernatant containing anot species showed that antibodies pass from the cells the supernatant to reach approximate equilibrium and from the supernatant to the cells. To test the la possibility under physiologic conditions, normal lymp cytes were allowed to incubate in vivo in their o lymph to which antibodies had been added. It again found that no absorption of antibodies by c took place.

Inasmuch as the function of the lymphocyte has n been known, these results are of interest from the p of view of cellular physiology, as well as that immunology.

Importance of Heredity in the Prognosis Febrile Convulsions. Dr. Samuel Livings and Dr. Laslo Kajdi, Baltimore.

During fourteen years approximately 800 patients w admitted to the epilepsy clinic of the Johns Hopk Hospital. All were referred to the hospital beca they had had seizures with such frequency as to g rise to the suspicion of epilepsy. In the course analysis of the cases it was noted that a not uncomm concomitant of the convusive state was fever. It considered a matter of interest to make follow studies of those patients in whom the first convulsi were febrile in order to collate whatever significant d might be at hand and to determine, if possible, standa or criteria on the basis of which a prognosis might formed. Of the total group of 800 patients there w 94 (over 10 per cent) whose first convulsions w febrile.

The age of onset of febrile convulsions has no bear on their outcome. Differences in race and sex are significant with respect to subjectivity to or chance recovery from this condition. The number of seizu experienced by a patient is significant; the rate of covery among patients having few seizures (less t twenty-four) is relatively high. Grand mal convulsi warrant a more favorable prognosis than focal c vulsions. The continuance of fever as an associate the spells is an excellent augury, since in this study patients whose attacks were always febrile returned time to normal.

The relationship between the hereditary background these patients and the persistence of their convuls behavior is both interesting and suggestive. It has b noted that the smallest per cent of recovery occurs the group showing an epileptic background and greatest per cent of recovery in the group having background of childhood convulsions only, while mean per cent of recovery is found in the group wit negative background. The following hypothesis is vanced as a tentative explanation of these observatio Individuals vary as to their convulsive thresho Physiologically the variations are determined by diff ences in functional stability of the cells involved in convulsive reactions. The degree of stability of a is at any instant fixed by its biologic background, the stage of maturation it has achieved and by the vironmental agents to which it has been and is be subjected.

A person born of epileptic family stock has a defect biologic background. A probable characteristic of "convulsive" cells is diminished vitality, and this char teristic will probably be permanent. He will, therefo have a low convulsive threshold, which will persist. will probably be epileptic. A person born of a

ject to childhood convulsions only is born with nglion cells whose convulsive threshold is low. The inution of the threshold of such a person, however, due to immaturity and thus will be only temporary. will probably not be epileptic. On the other hand, erson who comes of a family that is free of both epsy and childhood convulsions is endowed with cells normal stability. He has a relatively high convulsive eshold. If this person manifests convulsive behavior, is probably the result principally of an exogenous nt. But since his convulsive threshold is high, this nt must have been intense. Its violence or intensity y have caused some substantial damage to the nervous tem and so effected a permanent diminution of cell ility. The convulsive threshold will, accordingly, be manently lowered, and the person will be epileptic.

mparative Study of Methods of Treatment in Infantile Paralysis. Dr. William T. Green, Boston.

A comparative study was made of the first year's con-escence of a group of patients who had infantile ralysis in 1943 and who were treated by the Kenny thod and that of a similar group who had the disease 1941 and were treated by the method which was lved at the clinics of the Harvard Infantile Paralysis mmission. This survey was made with full recog-ion of the difficulties and defects in such a study and th appreciation of the variability of the disease in ividual patients and in particular years.

Similar criteria were used in including the patients in two series; all the patients were admitted to the ildren's Hospital within a few days after the onset d have been followed regularly throughout their con-escence, the muscles being examined regularly. There re 23 patients in each group. The Kenny technic s carried out by one of the experienced physical rapeutists on the staff of the hospital, who had had ining with Sister Kenny; the nursing care was ected by a nurse who had been similarly trained.

The recovery of muscular function was studied in ious ways. Curves were constructed representing an erage index of the return of total muscular function the two series. On analysis it was found that the ves of recovery in the two series showed little signifi-nt difference.

The involved muscles were then classified into groups ed on the degree of initial weakness, and the patterns recovery of these individual groups were observed. ain, there was little difference in the two series. uscles with an initial rating of "zero" did better in 1941 series; "poor" muscles had an identical pattern; air" muscles did slightly better in the 1943 series, the e treated by the Kenny method.

The status of the patients one year after the onset s evaluated in several ways. Patients treated by Kenny method are alleged to be more flexible n patients treated by other methods. When straight raising was used as one index of flexibility, the o series showed little difference; the 1941 group eraged 84 degrees and the 1943 group, 76 degrees. e average tightness of the heel cords was identical the two groups.

It is stated that weakness of abdominal muscles rely occurs in patients treated by the Kenny method. is observation I was unable to confirm: Fewer ients had residual abdominal weakness in the 1941 ies than in the Kenny group.

The patients in the groups were given a summary aluation at an examination which was performed one year after the onset. Sixty-one per cent of the 1941 series were considered normal or nearly normal; 57 per cent of the 1943 group—those treated by the Kenny method—were so designated. Twenty-six per cent of the 1941 series and 17 per cent of the 1943 group had mild to moderate minus disability. Thirteen per cent of the 1941 series and 17 per cent of the 1943 group had moderate to moderate plus disability. There were no patients with marked or with very marked disability in the 1941 group; there was 1 in each category in the 1943 group.

If the figures are reconsidered, it is apparent that 13 per cent of the 1941 series had moderate disability or worse, whereas 25 per cent of the patients treated by the Kenny method were in this classification. Although these findings are favorable to the 1941 series, the differences are not interpreted as necessarily significant and may be considered within the limits of variation which will be found in comparing two groups of patients treated by the same method.

It is concluded on these and other bases that the Kenny treatment is not revolutionary in its results. It is fair to state that from the Kenny treatment and from my experience with this method certain modifications in treatment have arisen which seem to be helpful in certain phases of the disease.

Determination of Concentration of Protein-Bound Iodine in the Serum as a Measure of Thyroid Activity. Dr. N. B. Talbot, Dr. A. M. Butler and Dr. A. H. Saltzman, Boston.

The experiments of Riggs and Man, Salter and others have shown that the concentration of protein-bound iodine in the plasma of serum is a good index of thyroid activity. While measurements of the plasma concentration of protein-bound iodine of normal adults and of adult patients with disease of the thyroid are available, few referring to children have been encountered. The present paper reports preliminary observations on the usefulness of this measurement in pediatrics and in the study of certain physiologic phenomena. The values reported were obtained on 4 cc. of serum with a colorimetric method of assay developed in our laboratory by modifying the methods of Riggs and Man.

The results obtained may be summarized as follows:

1. The normal values for children (average, 6.5 micrograms per hundred cubic centimeters; range, 4.5 to 8.5 micrograms per hundred cubic centimeters) correspond closely to those for adults.

2. Infants and children with primary hypothyroidism have abnormally low values; persons with hypothyroidism secondary to proved deficiency of the anterior lobe of the pituitary also have low values.

3. Children with hypothyroidism receiving standard doses of thyroid U. S. P. (1 to 2 grains [0.06 to 0.13 Gm.] per day) have normal values.

4. Most children with idiopathic dwarfism have normal values.

5. Persons with hyperthyroidism have abnormally high values. The fall in these values is parallel with the fall in the basal metabolic rate and the insensible loss of weight when thiouracil is given.

6. When normal adults fast for six days, their iodine values fall from normal to subnormal levels.

These findings supplement the available evidence that the concentration of protein-bound iodine in the serum is a useful, direct index of thyroid activity. This direct determination of thyroid function is perhaps par-

ticularly valuable for children, because the method of calculating thyroid function indirectly, from the basal metabolic rate, is frequently difficult to use and to interpret.

Maternal Isoimmunization in the Causation of Mental Deficiency. Dr. Herman Yannet and Miss Rose Lieberman, Southbury, Conn.

The occurrence of cerebral changes, known pathologically as kernicterus, is almost entirely confined to children with erythroblastosis fetalis. Demonstration of the importance of Rh isoimmunization in the causation of erythroblastosis fetalis makes it reasonable to assume a causal relationship between the cerebral changes and the process of isoimmunization.

It has been shown that there is no correlation between the severity of the manifestations of erythroblastosis and the occurrence of the cerebral damage, the pathologic changes in the brain having been demonstrated in children in whom the changes in the blood as well as the jaundice were minimal and were even considered within normal limits. It has, therefore, been postulated that a certain proportion of children with mental deficiency now diagnosed as "undifferentiated" because of lack of distinguising characteristics or of known etiologic factors, may possibly represent the results of maternal isoimmunization even when their histories as available do not indicate typical neonatal erythroblasttosis.

In a previous publication we showed that the incidence of Rh incompatibility in mother and patient (i. e., an Rh-negative mother and an Rh-positive child) was significantly higher for this undifferentiated group than for a control group consisting of children with defects of known classification, such as mongolism, cerebral palsy and birth trauma. In the present paper, in addition to reporting further studies on the Rh mechanism, we have investigated the possibility of incompatibility as regards the A and B factors. The results so far (over 200 children and their mothers have been studied) seem to indicate that maternal isoimmunization to the A and B factors may also be of significance in this respect. The previous studies on the Rh mechanism are also confirmed.

Second Session

Tuesday Morning, Sept. 26

Comparison of Various Types of Oil in the Treatment of Rickets. Dr. Donald J. Barnes, Detroit.

This paper reports results of studies of calcium and phosphorus balance made on 28 rachitic infants through two winters. In an attempt to estimate the minimal level of intake of vitamin D which would produce healing, 270 and 100 U. S. P. units respectively were used as the daily doses.

Except for a control group of 4 infants, who were observed without treatment for four to six weeks, the infants were divided into groups of 4 each, kept two weeks for observation without medication and then studied for six weeks while receiving medication. One group received 270 U. S. P. units of vitamin D as cod liver oil concentrate; another, 270 units as tuna liver oil; a third, 270 units as viosterol in oil; a fourth, 100 units as cod liver oil concentrate; a fifth, 100 U. S. P. units as tuna liver oil, and a sixth, 100 units as viosterol in oil. Eight weekly balance periods of three days each were studied for each group.

With vitamin D therapy the values for calcium retention increased tremendously, those for phosphorus retention increased less, the values for serum calci and phosphorus were higher and the level of ser phosphatase was reduced.

Calcium retention before therapy averaged 20.4 m per kilogram of body weight per day. One type response to treatment was a ceiling retention of fr 59 to 71 mg. per kilogram per day by the second a third weeks and a subsequent fall to from 48 to 52 m per kilogram by the end of six weeks. This type response was observed with the groups receiving 2 and 100 U. S. P. units of cod liver oil concentra 270 and 100 units of tuna liver oil and 270 U. S. units of viosterol in oil. The group receiving 100 un of viosterol in oil gave a different response, reachi an average maximum value for calcium retention of mg. per kilogram after six weeks of therapy. The gro receiving 100 units of viosterol in oil was the slow to respond and by statistical analysis showed the le significant rise in calcium retention.

It is concluded that within the limits of this expe ment cod liver oil concentrate was, for human infan more effective in producing calcium and phosphor storage than was viosterol in oil. It probably is su rior to tuna liver oil.

Mineral balance studies at levels corresponding to daily intake of 100 U. S. P. units of vitamin D pern distinctions to be drawn among these sources of vi min D on the basis of their effectiveness in the tre ment of rickets.

Effectiveness of Sulfadiazine and Antipertus Serum in Treatment of Pertussis. Dr. Wi liam L. Bradford, Miss Anne Brooks and D Chris P. Katsampes, Rochester, N. Y.

Although certain members of the sulfonamide gro of drugs have been used in the treatment and preve tion of the complications of pertussis, but little atte tion has been given to their effect on the speci organism, Hemophilus pertussis. Since there is e dence that the specific organism itself is an import cause of the ordinary pulmonary lesion in whoopi cough and since both sulfadiazine and antiserum a known to modify favorably the course of the expe mental disease in the rat and in the mouse, it seem important to test the therapeutic effectiveness of the agents individually and in combination.

This report describes the results of such a study the experimental murine disease and of the natur disease in infants. In the study of the experimen disease the method employed was as follows: Thr week old Swiss mice were inoculated intranasally wi different doses of a suspension of H. pertussis. Twent four hours after the infection the test groups we given sulfadiazine or antiserum either alone or combination. The sulfadiazine was injected intr abdominally twice daily in a 0.5 per cent solutio The total daily dose was 0.1 Gm. per kilogram body weight. The treatment was continued for sev days.

Two immune rabbit serums, one antibacterial and t other antitoxic, were given intra-abdominally twent four hours after the infection, and daily injections we continued for seven days. The dose was 0.2 cc. of 1 : 10 dilution of the serum.

The criteria employed to measure the therapeut effect of the agents were (*a*) mortality and (*b*) clea ance of the organisms from the lungs of the survivi mice.

The results indicated that sulfadiazine, the antiba terial serum and the antitoxin each protected mi against experimental pertussis when administer

nty-four hours after the infection. Each of these nts brought about disappearance of the organisms n the lungs of the surviving mice, but this effect not always reproducible. When a combined form herapy, consisting of administration of either the with the antibacterial serum or the drug with antitoxin was used, there were effective clearance he organisms from the lungs and protection of the against death.

he practical application of the combined therapy tested on infants with early pertussis. Four groups 11 infants each were studied: The first group ived sulfadiazine, the second received antibacterial m, the third received both drug and serum and the rth served as controls. Because it was obviously cult to assess the effect of therapy on the clinical rse of the disease, attention was focused on clear- of the organism from the nasopharynx, as deter- ed by repeated nasopharyngeal cultures. While adiazine and the antibacterial serum each caused nite clearance of the organism from the naso- ynx, the combined therapy resulted in a more mpt and lasting effect.

iatric Uses of Standardized Curare. Dr. Charles F. Church, New Brunswick, N. J.

urare induces muscular relaxation by direct action the neuromuscular junction, where it neutralizes ylcholine released at the time of motor nerve dis- rges. This characteristic action makes purified dardized curare a drug of great value in medicine, special uses in pediatrics.

he botanic source of curare has been identified as ndodendron tomentosum, which is found in certain s of the Amazon basin. From extracts of this t a crystalline alkaloid has been isolated by Dutcher Wintersteiner and identified as d-tubocurarine. de preparations of curare are purified by extraction h alcohol and standardized by biologic test. When rabbit head drop method of assay is used, results reproducible with a high degree of accuracy. The mercial preparation (intocostrin, manufactured by R. Squibb and Sons) is purified and standardized contain the equivalent of 20 mg. of standard curare cubic centimeter. It is tested for sterility, chronic icity and presence of pyogens. Curare is not effec- when given by mouth but must be administered intramuscular or slow intravenous injection.

tandardized curare has been used extensively in ropsychiatry to soften convulsions in shock therapy thus eliminate the risk of fractures. It is also ful as a diagnostic agent in distinguishing myas- nia gravis.

he special pediatric uses of standardized curare are an agent to induce muscular relaxation in surgical sthesia and as an aid in the treatment of spastic alysis. When curare is used in combination with anesthetic such as cyclopropane, complete relaxa- n of the muscles may be obtained at will without ort to deeper anesthesia. The depression of respira- n which may occur in a patient who is under the luence of curare can be controlled by use of artificial piration and/or by injection of prostigmine methyl- fate (1 to 2 cc. of a 1 to 2,000 solution).

n the treatment of spastic paralysis (birth palsy) muscular relaxation obtainable through injection of rare is of definite value as an aid in muscle train- . This treatment provides the child with a sense muscular relaxation and control which lasts much ger than the physiologic effect of the curare itself.

Immunity in Mumps: Experiments on Vaccination of Human Beings with Formaldehyde-Treated Mumps Virus. Dr. Joseph Stokes Jr., Dr. John F. Enders and Dr. Elizabeth P. Maris, Philadelphia, and Dr. Lewis W. Kane, Boston.

Since methods for determining susceptibility and immunity to mumps have been developed for both monkeys and human beings and since mumps virus vaccine when used in monkeys has been shown to cause a rise in antibody titer and an increased resistance of the monkey on exposure to active virus, experiments on vaccination were undertaken with groups of human beings.

Formaldehyde-treated vaccine was given subcutaneously to two groups of children. Subsequent exposure was assured by injection or spraying, after fourteen to seventeen days, of a measured suspension of active mumps virus into one parotid duct of each vaccinated person and of each of a suitable group of unvaccinated susceptible and nonsusceptible controls. Three types of response were noted. In the susceptible controls typical mumps developed. The nonsusceptible controls and the vaccinated controls, in whom appreciable antibody titers had developed before challenge, showed an immune reaction characterized by early swelling of the inoculated gland, by prompt subsidence and by involvement of no other gland. In general the vaccinated children who showed slight or, in some instances, no rise in antibody titer gave a somewhat prompt response, with mild swelling, which subsided quickly, and with occasional involvement of other glands than the inoculated parotid. This reaction may be interpreted as an accelerated response. Two vaccinated persons whose serums appeared to have no increase in antibodies had average incubation periods and had typical multiglandular mumps, similar to that observed in unvaccinated susceptible persons.

The challenge method of study seems to provide suggestive evidence that immunization of susceptible human beings with formaldehyde-treated mumps vaccine may be a means of curtailing epidemics of the disease. The determination of susceptibility and response to immunization may be satisfactorily evaluated through use of complement fixation tests and cutaneous tests.

Clinical Significance of Yellow Staining of the Vernix Caseosa, Skin, Nails and Umbilical Cord of the Newborn. Dr. Stewart H. Clifford, Brookline, Mass.

Fifty-seven living infants were studied at the Boston Lying-in Hospital in an effort to discover the clinical significance of a yellow staining of their vernix caseosa, skin, nails and cord, which was noted at birth. Their mortality rate was 12 per cent. Only 11 (20 per cent) of the group had erythroblastosis fetalis. (During the period of this study a total of 26 patients with erythroblastosis were encountered, in 15 [60 per cent] of whom yellow staining was not noted at birth.)

The remainder of this communication is devoted to a study of the 46 yellow-stained babies who did not have erythroblastosis fetalis. Their morbidity rate was 60 per cent, and their mortality rate was 6 per cent.

Clinically, the symptoms encountered were asphyxia at delivery, atelectasis, cyanosis, hypotonia and hypertonia, hyperpyrexia, anemia, petechial hemorrhage, hematemesis, dehydration, convulsions, increased intracranial pressure, excessive mucus in the resipratory tract and vomiting.

The physical findings were yellow staining of the vernix caseosa, skin, nails and umbilical cord, pulmonary atelectasis and enlargement of the spleen and the liver. Twelve per cent had red cell counts of less than 4,000,000, and in 30 per cent the erythroblasts comprised above 16 per cent of the total number of nucleated cells.

The mothers of babies with yellow vernix were considerably older and had had more pregnancies than the mothers in the general hospital population. Forty per cent had serious complications of their current pregnancies: Seventeen per cent had postmature babies; 9 per cent had toxemia; 7 per cent had had repeated attempts at external version during pregnancy, and 7 per cent had premature separation of the placenta, latent syphilis or chronic bronchiectasis.

For 93 per cent of the babies with yellow vernix no abnormality of the fetal heart had been recorded during labor, in spite of the fact that 28 per cent required vigorous resuscitation at birth.

Eighty-four per cent of the placentas, umbilical cords and fetal membranes were reported by the pathology department to be stained yellow or green—a condition interpreted as indicating intrauterine fetal asphyxia.

Only 3 per cent of 37 placentas examined were reported as normal. The remainder showed evidence of premature separation; old focal necrosis with calcification in the decidua; antepartum necrosis of many villi; decidual necrosis, with obliteration of the fetal vessels; thrombosis in the decidual sinusoids; chorionitis, with a loose, edematous chorionic plate containing a large number of monocytic cells whose cytoplasm was filled with a fine brown pigment, and massive hemorrhage in the stroma of the cord with slight edema and hypoplasia of the placenta.

Based on this evidence, the hypothesis is advanced that the yellow vernix syndrome is the result of episodes of fetal asphyxia occurring days or weeks before the onset of labor and resulting in asphyxial injury to the fetus, accompanied with liberation of meconium into the amniotic fluid. With time the bile pigments stain the vernix, cord, nails and skin the characteristic golden yellow.

These observations suggest that the principal cause of the prenatal fetal anoxia is to be found in the placenta, and microscopic examination of this organ may well reveal the type of pathologic process responsible.

Effect of Local Irritant on Skin of Dogs: Influence of Fat in Diet on Lipids of Serum and Tissues. DR. ARILD E. HANSEN and DR. HILDA F. WIESE, Minneapolis, and MR. JENNINGS KOODA, Galveston, Texas.

The purposes of this study were to note the effect of fat in the diet on the ability of the skin of dogs to resist local irritation and to determine whether or not changes occurred in the serum or tissue lipids under these conditions. During five experimental periods four groups of animals were used. One dog in each group received fresh lard as a source of dietary fat, and 1 was maintained on a diet low in fat (0.16 per cent). Daily applications of an acetone solution of croton oil were made over comparable areas on the dorsum of each animal.

Adult dogs were used in the first two experiments. With the application of a 5 per cent solution of croton oil on 2 adult dogs heavier eruptions developed on the animal which was receiving the low fat diet than on the animal which was receiving lard. However, when a 3 per cent solution of croton oil was used on 2 other adult dogs, little difference in the reaction of the sk was noted.

Subsequent studies were made on young dogs wh were litter mates, using the 3 per cent solution of cro oil. The young animals receiving the low fat d showed the flaky desquamation of the skin which characteristic of young dogs maintained on such a di In this series there were three experimental perio from six to nine weeks in duration. In each instan the treated area of the skin of the animals fed the l fat diet showed definite erythema, some thickeni papules, vesicles with exudation and crusting. The hei of the reaction occurred in three to four weeks. Sim larly treated areas of the animals receiving lard in diet remained clear.

Periodic determinations of the serum lipids were ma for 1 pair of the young dogs, for which the total fa acids, the acetone-soluble fatty acids, the acetone-insolu fatty acids and their iodine numbers and the cholest and cholesterol esters were determined. In the anim receiving fat there was little change in the amount character of the serum fatty acids during the expe mental periods. Some changes in the serum fat of animal fed the low fat diet were noted. The m noticeable effect was a decrease in the iodine numb of the fatty acids in the various fractions. Analyses the skin and subcutaneous tissues for lipids were ma before and during the experimental periods. No chan was found in the iodine number of the fat extract from the skin of either animal. The iodine number the fat in the subcutaneous tissue of the dog fed low fat diet increased from 56 to 70 and that of the d receiving lard from 65 to 71.

Relative Efficiency of Three Forms of Intrav nously Administered Nitrogen on Nitrog Balance and Amino Acid Excretion. DR. WA REN M. COX JR. and MR. ARTHUR J. MUELL Evansville, Ind.

To measure the relative nutritional efficacy of pare terally administered nitrogen, 3 dogs were fed a di low in protein; they received 50 calories of protein p kilogram of body weight for approximately two mont The amount of nitrogen calculated to reestablish nitr gen equilibrium exactly was intravenously administer for successive periods of ten days each. Three sour of nitrogen were compared: (1) an enzymic hydroly of casein and pancreas (Amigen); (2) a mixture of t ten essential amino acids (Madden V_u), and (3) a mi ture of the ten essential and ten unessential amino ac (McCoy, Meyer and Rose, *J. Biol. Chem.* **112**:283, 193 believed to represent the composition of casein. An equ amount of nitrogen in each form was administered. Af thirty days of intravenous supplementation the nitrog injection level for each supplement was doubled; subs quently, the levels of the first two supplements w quadrupled and octupled. Values for nitrogen balan plasma protein and albumin, hematocrit determinatio weight and urinary amino nitrogen before and after a hydrolysis were determined for the one hundred a seventy-four days of the experiment.

Initial levels of 0.055, 0.099 and 0.106 Gm. of nitrog per kilogram of body weight were calculated as t minimum required to reestablish nitrogen balance. this level the mixture of the ten essential amino ac was slightly more efficient in establishing nitrogen b ance than the hydrolysate and greatly superior to t mixture containing twenty amino acids. At higher lev the hydrolysate was considerably more efficient. T

erage nitrogen balances for the 3 dogs, expressed as rams of nitrogen per day, were as follows:

Nitrogen Source	Nitrogen Level			
	Minimal	2 x	4 x	8 x
drolysate	−0.19	+0.60	+1.48	+3.33
dden Vu	+0.16	+0.78	+0.97	+1.04
Coy, Meyer and Rose ixture	−0.34	±0.00	—	—

The level of total plasma protein and of plasma umin rose slightly during the injections, coincidentally ith a gradual unexplained fall in the hematocrit read- g. Changes in weight paralleled supplementation with trogen; with the two lower levels of nitrogen the fall weight was arrested, and with the two higher levels the dogs gained weight.

The urinary excretion of amino nitrogen was two to ree times as great with the crystalline amino acid ixtures as with the hydrolysate. This difference was t caused by differences in rates of injection, for the tes were similar. The excretion of peptide nitrogen ith the hydrolysate almost balanced the loss of amino id from the crystalline mixtures, since the total figure r amino nitrogen after acid hydrolysis of the urines om the latter was only slightly greater than that from e hydrolysate.

The amounts of essential amino acids given in the rious forms differed. As compared with the hydrol- ate, the McCoy, Meyer and Rose mixture was de- ient in threonine and leucine, and the Madden Vu ixture supplied almost twice as much of each essential id. Presumably, when this mixture was given, some sential acids were employed by the body to make the -called unessential acids. On the other hand, the drolysate may not have contained the optimum amount some essential amino acid, since at low levels it was t quite so effective as the mixture of the ten essential ino acids. It is not clear why the hydrolysate was perior to the crystalline mixture at higher levels of take; perhaps the so-called unessential acids are really sential when no adequate source of them is available.

cute **Idiopathic Porphyria with Repeated Attacks of Peripheral Neuritis: Treatment with Liver Extract.** DR. HARRIET G. GUILD, Baltimore.

This report concerns a patient with acute idiopathic rphyria. The disease was intermittently active, with tremely severe manifestations, for six years but has the time of writing been completely quiescent for ven years, while the patient has been receiving con- uous therapy with liver extract.

The onset of the disease occurred in September 1931, hen she was not quite 9 years of age, with a brief ness characterized by abdominal pain, convulsions and ssage of red urine containing a trace of albumin and few casts, which led to a mistaken diagnosis of phritis. After her recovery the red color frequently appeared in the urine, but, except for a slight con- lsion during convalescence from tonsillectomy three onths after her recovery from the initial illness, she mained well until January 1933. At this time there as again sudden abdominal pain, followed by severe nvulsions, transient loss of vision and development peripheral neuritis, with acute symptoms of about o weeks' duration. There was gradual improvement ter this until April, when another attack was ushered by sudden extreme irritability, pain and swelling in e feet, abdominal pain, nausea and vomiting; there llowed diplopia, convulsions, difficulty in voiding and defecating, recurrence of the peripheral neuritis and delirium with visual hallucinations and changes in personality. In this condition she was referred to the Harriet Lane Home, Baltimore, where the demonstration of porphyrins in the red urine established the diagnosis of acute porphyria. Tachycardia and, later, hypertension were also noted. The blood picture was normal, and the spinal fluid showed no abnormalities. Improvement occurred within a few weeks, and the child regained the power to walk and write, although the foot and wrist drops persisted.

Throughout the next four years the disease continued to follow a typical course, with a series of attacks, many of which seemed to be precipitated by infection of the upper respiratory tract. In some attacks the symptoms were limited to abdominal pain, vomiting, difficulty in voiding and defecating, tachycardia and hypertension; in others mental depression and peripheral neuritis were added. At times paralysis was so extensive that the patient could not turn over in bed, while involvement of the diaphragm actually threatened life. Porphyrins, chiefly uroporphyrin I with some coproporphyrin I, were excreted in the urine throughout the illness, although they decreased in amount during the intervals between attacks. Urobilin and urofuscin were also demonstrated, in addition to an unidentified pigment that seemed to appear only during attacks. The urine was otherwise normal. The blood picture remained normal except for occasional slight leukocytosis, occasional mild eosinophilia and a persistently elevated sedimentation rate. A moderately elevated level of nonprotein nitrogen in the blood, a frequently abnormal levulose tolerance curve and an elevated cholesterol level were the only other significant findings.

From the fall of 1934 through the spring of 1935 attacks were so frequent and severe that there was only partial recovery from one before the next arrived, and it seemed as though the patient could not possibly survive. At this point, because of similarities between this disease and pernicious anemia, in spite of the absence of anemia, intramuscular injections of liver extract were started. Lilly's purified extract was given in doses of 2 cc. a day for four days, then 1 cc. a day for ten days and then 1 cc. twice a week and finally once a week. Apparent improvement, with only two mild attacks (during the course of which daily injections of 1 cc. were temporarily resumed) in the next six months, suggested that an effect was being achieved. Sudden development of two more severe attacks in rapid succession led to the decision to continue the daily injections of liver extract without interruption for an indefinite period. After the institution of this regimen there were no more severe attacks. During the few mild ones that occurred, the amount of liver was gradually increased until the patient was finally established on a dose of 3 cc. a day. Since then attacks have ceased and with continued treatment the patient has remained well up to the time of writing except for some residual atrophy of the hands and feet and slight impairment of renal and hepatic function; pigments can, however, still be demonstrated in the urine.

While the apparent effect of liver therapy may be coincidental, laboratory evidence that excretion of porphyrin in cases of congenital porphyria is modified by injection of large doses of liver extract offers support for a causal relationship. Even though pigments other than the porphyrins may be concerned in the symptomatology, it is probable that such substances arise from the same defect in metabolism and that any therapy

affecting the formation of porphyrins would affect the other pigments as well. Furthermore, this patient seems to have been the sickest person on record who survived and remained free from active symptoms for so long. Reports in the literature regarding the futility of treatment with liver extract are difficult to evaluate because of the lack of information regarding extracts used, doses given and duration of therapy. It is recommended that intensive treatment with daily injections of large doses for an indefinite period be given further trial in treating patients with this form of porphyria and perhaps also in treating those with congenital porphyria.

Congenital Malformations of the Eyes Induced with Maternal Deficiency of Vitamin A. Dr. Josef Warkany and Miss Elizabeth Schraffenberger, Cincinnati.

It has been repeatedly observed that the offspring of animals fed deficient diets were born blind. Blindness in calves associated with constriction of the optic nerve, probably of nutritional origin, was reported by Moore and his co-workers. The blindness of pigs born to sows fed a vitamin A–deficient diet, reported by Hale, was caused by an entirely different mechanism. This author reported anophthalmos, microphthalmos and other congenital malformations and proved that heredity could be ruled out as the cause of these defects. For obvious reasons it seemed desirable to reproduce and follow up these observations in a small laboratory animal, for no corresponding findings have been reported in rats.

We have recently observed congenital malformations of the eyes in the offspring of rats that were raised on a diet containing measured small amounts of carotene and those of rats bred on a diet entirely free of carotene and vitamin A. Within a week the rats fed the vitamin A–free diet showed pronounced signs of nutritional deficiency, and their reproductive performance was poor. Twelve of the first group of 20 females bred, but only 3 carried their litters to or near term. The three litters consisted of 19 dead young, all of which had normal eyes. In 14 of these young the abnormality could be recognized by external inspection. Instead of the closed eye present in the normal newborn rat, a red, irregular depression was seen in the region of the eye. Sections showed complete disorganization of these abnormal eyes. They were externally covered by a thick membrane, which represented a fusion of the eyelids and the cornea. The conjunctival sac, the anterior chamber, the iris and the ciliary body were absent. In the posterior part a cleft was seen in the retina, and through this cleft there entered mesodermal tissue, which spread out behind the lens and took the place of the vitreous. This is a typical coloboma, a true malformation of the eye. In the early stage of development the eye cup is open on its inferior surface, and through this fissure enter the hyaloid artery, the mesoderm associated with it and the fibers of the optic nerve. When the fissure closes, the mesodermal tissues disappear as the vitreous develops. If development is arrested, the fetal cleft and the connective tissue persist.

In a second series of experiments identical results were obtained. In addition, a number of fetuses were procured all of which had abnormal eyes. Coloboma of the retina and persistent tunica vasculosa lentis could be recognized in 16 day fetuses. These experiments were done with rats of the Sprague-Dawley strain, a strain with which we have worked for many years and in which we have not seen any comparable defects of the eyes when the animals were fed an adequate diet.

SUMMARY

Severe vitamin A depletion in the mother may re in congenital ocular defects in the young. Malfor tions such as coloboma retinae, persistent tunica v culosa lentis, fusion of the eyelids and cornea absence of the anterior chamber of the iris and ciliary body were observed. These experiments on confirm in principle the previous findings of Hale in p Vitamin A is necessary not only for the function for the formation of the eye.

Waterhouse-Friderichsen Syndrome: Its Tre ment with Adrenal Cortex Extract. Dr. M garet H. D. Smith, Baltimore.

Acute circulatory collapse associated with gr hemorrhage into the adrenals is seen in septicemia, p ticularly in meningococcic septicemia. Some cases circulatory collapse, however, could not be explain because gross hemorrhage was not found at autop Recently Rich has drawn attention to extensive fo necroses of the adrenals occurring in such cases. Th lesions, which vary in extent and severity, would se to provide a logical explanation for the clinical var tions seen. Some patients with meningococcemia sh a temporary drop in blood pressure at the onset of illness. Others, particularly infants, show an extens purpuric rash with severe shock and die within two to twenty-four hours of the onset of symptoms. A th group includes those patients, most commonly ol children and young adults, who may survive for two three days with marked hypotension, only to die at end of that time.

Three cases were briefly presented. One was that a 23 year old woman, who was admitted to the hosp in a state of collapse after an illness of ~~eighteen~~ hou Her blood pressure was 70 systolic and 45 diasto Despite intravenous injection of fluids she died eight hours later. Her adrenals showed focal necroses w "tubule-like formation."

The patient in the second case was similar. She a 26 year old woman who had been ill for twelve ho before her admission to the hospital. She showed p nounced restlessness and cyanosis, and her extremi were clammy. She had a tender mass in the right fla which, it was thought, might represent a hemorrh into the adrenal. Despite intravenous injection fluids and administration of moderate doses of corti extract, her blood pressure fell rapidly from 84 syst and 50 diastolic to 60 systolic and 0 diastolic, and levels of blood potassium and nonprotein nitrogen r She was then given 65 cc. of adrenal cortex extr intravenously within a two hour period. The respo was dramatic. Maintenance doses of cortical extr were necessary for a week.

The patient in the third case was a 1 year old infa who appeared only moderately ill on his admissi Blood was obtained immediately for chemical determi tions, and when he had a circulatory collapse a f hours later, repeat determinations showed that the le of nonprotein nitrogen had risen from 36 to 72 mg. hundred cubic centimeters, the level of potassium risen from 4.7 to 7.9 millimols per hundred cubic ce meters and the carbon dioxide–combining power of blood had dropped from 40 to 35 volumes per c After intravenous injection of adrenal cortex extr and of large amounts of a solution of dextrose sodium chloride, he recovered.

Other patients have shown similar changes in the lues for the chemical constituents of the blood, and a mber have responded equally well to treatment.

Therapy consisted in all cases of intravenous injection sulfonamide drugs and of large amounts of a solution sodium chloride and dextrose. These measures alone em to produce great improvement in patients with ld forms of the disease. In patients with severe rms of the disease immediate and dramatic improvent followed the use of large doses of adrenal cortex tract given intravenously (i. e., 15 cc. as an initial se for a 10 year old child, repeated as often as necesry to sustain the blood pressure). Desoxycorticosterone has been found unsatisfactory, and I no longer use it.

Whether these patients die of "toxemia" or of acute adrenal insufficiency is as yet unknown. However, the changes in the electrolytic pattern of the blood and the tendency to hypoglycemia and azotemia, as well as the clinical picture, are compatible with, if not pathognomonic of, adrenal insufficiency. The response to adrenal cortex extract is striking. I feel, then, that acute adrenal insufficiency is at least an important factor in causing death in these patients and that suitable replacement therapy will save a number who would otherwise die.

Obituaries

LOUIS FISCHER, M.D.
1864-1944

Dr. Louis Fischer, one of the pioneer pediaicians of the country, died in New York city April 9, 1945, at the age of 80. After graduing from the New York College of Pharmacy 1882, he received his M.D. from New York niversity Medical College in 1884 and started e practice of general medicine at the age of . Bacteriology was not included in the medical rriculum of his time. When he read of the w science, he went abroad and studied in eichselbaum's laboratory. A few years later, hile he was in Berlin, diphtheria antitoxin was oduced by Behring and von Wernicke. The illiant therapeutic results of "Anti-Toxine," as was called, made medical history. Dr. Fischer ought some of the serum with him and successlly used it in treatment and reported the first cases of its use in America in October 1894. During subsequent trips abroad he studied with Baginsky and later with Finkelstein in Berlin and von Pirquet in Vienna and helped to bring to the United States knowledge of infant feeding obtained from European clinics. Dr. Fischer was attending physician at Willard Parker, Sydenham and Riverside Hospitals in New York city. He later became associated with the Heckscher Foundation for children and was for many years a member of the medical advisory board of the New York City Department of Health and of numerous child welfare organizations. His interest in pediatrics never lagged, and in his seventy-fifth year he was granted recognition by the recently formed American Board of Pediatrics. He was always willing, and deemed it a privilege, to help the younger generation of pediatricians.

Book Reviews

The Electrocardiogram: Its Interpretation and Clinical Application. By Louis H. Sigler, M.D., F.A.C.P. Price, $7.50. Pp. 403, with 203 illustrations and plates. New York: Grune & Stratton, Inc., 1944.

In his preface the author states that he has attempted to present the subject of electrocardiography in a practical and concise manner, and he has achieved this objective admirably. He emphasizes the fact that the electrocardiogram is merely a record of the electrical potential of the heart and that the variations from the normal may have a variety of causes. He not only points out the variations due to pathologic conditions but describes the changes which may be due to various constitutional and toxic states.

He divides his book into twenty-five chapters, each dealing with a particular phase of electrocardiography. His discussion of the theory in the first chapter is adequate and clear. Other chapters deal with the various arrhythmias, the patterns of electrocardiographic variations due to coronary disease and the other variations indicative of myocardial involvement or physiologic change. The illustrations are well chosen and show the classic patterns in the types of abnormalities commonly encountered. However, in his chapter on the "Effect of Drugs and Chemicals on the Electrocardiogram" one wishes that he might have presented illustrative curves. His description of the changes due to digitalis are fairly accurate but not as impressive or valuable as a graphic illustration. The last chapter is devoted to a discussion of precordial leads. This chapter is rather lengthy and has some very good illustrations of the normal pattern and of variations due to anterior and posterior infarctions in the six standard precordial leads. However, he gives no illustrations of the patterns found with right and left axis deviation or with the various types of intraventricular block. The common use of the precordial leads makes an understanding of these patterns essential to the proper interpretation of the electrocardiogram. The author also fails more than to mention the fact that in children chest leads may show an inversion of the T wave in normal hearts. He, in fact, gives little discussion of the variations of the electrocardiogram in children, although he does mention that there is a definite variation with age.

One wishes, also, that he had devoted more space to the discussion of electrocardiographic variations with rheumatic heart disease, both in children and in adults.

In general, the book is a good and clear exposition of electrocardiography and will be of value for the purpose of teaching and as a reference book for students. The bibliography is fairly adequate and includes recent publications. The book also contains an index which is helpful.

Patients Have Families. By Henry B. Richardson, M.D. Price, $3. Pp. 408. New York: Commonwealth Fund, 1945.

This book, which is a thoughtful summary of the relationship of the patient to the family, is a result of studies made at Cornell University Medical College in cooperation with the faculties of public health, medicine and psychiatry and the New York Hospital, w its social service department and with the Commu Service Society.

Dr. Richardson considers the subject in its br aspects, beginning his thesis with the relationship several families to the hospital, both with its outpati and with its inservice facilities. In this part of book he shows how definitely related illness is to family status, medical, economic and social.

In a chapter on "Family Equilibrium" he shows factors which characterize the interrelationships of p sons as members of the family. He speaks of imi tion, identification, dominance of individuals, fan focus, motivations and cultural effects. After giv illustrations of these factors in the family life of act patients, he goes on to explain the role of the fam physician in handling situations and in carrying o this responsibility to the hospital.

The rest of the book is devoted more or less to various persons interested in patients as parts of fa ilies, namely, the psychiatrist, the case worker, medical social worker and the public health nurse. these chapters he explains the functions of each these workers in managing family situations. In t part of the book, too, considerable space is devoted the practical aspects of the family as it exists in w time today and to special technics.

To the thoughtful physician, Dr. Richardson's bo suggests many questions which if carefully thou through cannot but increase his understanding of t difficulties patients have to surmount in these hec days. It outlines the physician's duties in a broad field than "treatment of disease" and emphasizes ag that physicians treat persons, not diseases, and th these persons are modified, as well as motivated, their families. For this reason, the book should carefully read by every pediatrician, for no one is inf enced more by family relationships than a child by family.

The book is interestingly written, but it cannot read through at one sitting; it requires a great d of digestion, but the man who takes the time to stu it will be amply repaid.

Atlas of the Blood in Children. By Kenneth Blackfan, M.D., and Louis K. Diamond, M.D., wi illustrations by C. Merrill Leister, M.D. Price, $ Pp. 320, with 70 colored plates. New York: Co monwealth Fund, 1944.

The first 145 pages of this book are devoted to description of the blood cells in health, the erythrocyt in anemia, the leukocytes in disease, leukemia and t platelets. While this discussion of the physiology a pathology of the blood is necessarily brief, it contai all that is essential for any worker on blood to kno It is as concise and readable a discussion as this r viewer has ever seen. There is also a complete bib ography, if more details of the blood are desired.

The final part of the book contains the colored plat illustrating the diseases of the blood discussed. On t page opposite each is a line drawing to identify t pathologic cells which typify the disease. To say th

ese plates are excellent is an under statement. There simply no comparison between these perfect examples what one actually sees under the microscope and the ddy messes presented by most textbooks as examples blood pathology.

The authors may well be proud of this book. It is at pediatricians, general practitioners and hematolo- ts have been longing for and should be in the hands every one who wishes to see excellent portrayals of blood cells in disease.

e Abortion Problem. Proceedings of the confer- ence held under the auspices of the National Com- mittee on Maternal Health. Edited by Howard C. Taylor Jr., M.D. Price, $2.50. Pp. 182, with 24 tables. Baltimore: Williams & Wilkins Company, 1944.

This little book records the proceedings of a most teresting conference, participated in by physicians, yers and social workers, together with the health mmissioner of a large city and an eminent embry- gist. The causes of abortion, its prevention and atment were discussed by the medical participants. udies were presented indicating the prevalence of rtion in various strata of society and dealing with social and economic aspects. An interesting portion the report is the contribution of John H. Amen, dis- t attorney of Kings County, New York, in which explains the obstacles to effective legal control of rtion.

The question is most thoroughly gone into, particu- ly from the sociologic and economic standpoints, with good deal of information concerning the views held ncerning it by members of the bench and bar.

A summary of the work of the meeting by Howard Taylor Jr. concludes the book. The book will be rth reading by any one who is seeking knowledge in fields named.

Medical Uses of Soap. Edited by Morris Fishbein, M.D. Price, $3. Pp. 182, with 41 illustrations. Philadelphia: J. B. Lippincott Company, 1944.

This is an excellent collection of articles, a symposium dealing with the medical uses of soap. Each of the ten authors has previously contributed to the literature on this subject, and each one has handled his assignment well.

There are excellent chapters on the chemistry of soap, including its manufacture, the normal effects of soap on the normal skin, the unusual or abnormal effects of soap on the normal skin, the effects of soap on the diseased skin and the effects of soap on the hair. Other chapters deal with soaps for industry and the industrial worker, soap for shaving, cutaneous detergents other than soap and the medical uses of soap.

The book is full of useful information. All of the chapters are written in a clear, concise manner, and the text is easily readable. The book is printed on good paper with large, legible type, and there are 41 excellent photographs.

It would seem to this reviewer that this publication deserves a place on the bookshelf of every dermatologist and every general practitioner. It will enable each one of them to answer more readily many of the common inquiries received by the physician from the patient.

News and Comment

GENERAL NEWS

American Board of Pediatrics, Inc.—Fall examinations are scheduled as follows:

Written examination, locally, under a monitor, Oct. 19, 1945.

Oral examination, New York, Dec. 7 and 8, 1945.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Charles F. McKhann, University Hospital, Ann Arbor, Mich.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Section on Pediatrics

President: Dr. Vicente Laro.
First Secretary: Dr. Armando de Arruda Sampalo.
Second Secretary: Dr. Luiz Augusto de Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. L. G. Parsons, 58 Calthorpe Rd., Five Ways, Birmingham.
Secretary: Dr. Donald Paterson, 27 Devonshire Pl., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaasbolwerk 14ª, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratisla
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Tim
Six times year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., Lond
W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., Lond
W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Fri
of each month, 4:15 p. m.

Palestine Jewish Medical Association, Sectio of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Av
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

Sociedad Cubana de Pediatria

President: Dr. Angel A. Aballí Arellano, 17 No. 6
Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospi
Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Merced
Habana. Time: Last Wednesday of every month.

Sociedad Mexicana de Pediatria

President: Dr. Fernando López Clares, 12/a. Medel
191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles
Mexico.

Sociedad de Pediatría de Santiago de Cuba

President: Dr. Antonio Beguez Cesar, Sagarra 1
Santiago de Cuba.
Secretary: Dra. Susana Texido Vaillant, Padre P
57, Santiago de Cuba.

Sociedad Venezolana de Puericultura y Pediatr

President: Dr. E. Santos Mendoza.
Secretary: Dr. P. Oropeza, Hospital de Niños, Carac

Société de Pédiatrie de Paris

President: Dr. B. Weill-Hallé, 49 Avenue Raymo
Poincaire, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Cler
Paris, France.
Place: Hôpital des Enfants Maladies, 49 Rue de Sèvr
Time: 4:30 p. m., third Thursday of every mon

Uruguyan Society of Pediatrics

President: Dr. José Alberto Praderi, Eduardo Aceve
1132, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Mon
video.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. John Aikman, 184 Alexander S
Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blv
Memphis, Tenn.
In compliance with the request of the Office of Defe
Transportation and in the interest of the national w
effort a meeting will not be held in 1945.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

American Academy of Pediatrics

sident: Dr. Joseph S. Wall, 1864 Wyoming Ave. W., Washington, D. C.
retary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

American Hospital Association, Children's Hospital Section

irman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
retary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

American Pediatric Society

sident: Dr. James L. Gamble, 300 Longwood Ave., Boston.
retary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

Canadian Society for the Study of Diseases of Children

sident: Dr. R. R. Struthers, 906 Drummond Medical Bldg., Montreal.
retary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

sident: Dr. Edward M. Bridge, 219 Bryant St., Buffalo, N. Y.
retary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia 46.

SECTIONAL

Intermountain Pediatric Society

sident: Dr. Robert Alway, University of Utah School of Medicine, Salt Lake City 2.
retary-Treasurer: Dr. L. Paul Rasmussen, 1020 Boston Bldg., Salt Lake City 1.
ce: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

sident: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
retary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
ce: Boston Medical Library. Time: Four meetings year, occurring from September to May.

North Pacific Pediatric Society

sident: Dr. M. L. Bridgeman, 1020 S. W. Taylor t, Portland, Ore.
retary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

Northwestern Pediatric Society

sident: Dr. George B. Logan, 102 Second Ave. W., Rochester, Minn.
retary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
ce: Minneapolis, St. Paul, Duluth and Rochester. ime: January, April, July and October.

Rocky Mountain Pediatric Society

sident: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
retary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

Alabama Pediatric Society

President: Dr. Amas Gipson, 948 Forrest Ave., Gadsen.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.

Arizona Pediatric Society

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. William C. Deamer, University of California Hospital, San Francisco.
Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

Florida State Pediatric Society

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. A. Clement Silverman, 608 E. Genesee St., Syracuse.
Secretary: Dr. Albert G. Davis, 307 Gas and Electric Bldg., Utica.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Charles F. McKhann, University Hospital, Ann Arbor.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. John L. Gedgoud, University of Nebraska Hospital, Omaha.
Secretary-Treasurer: Dr. Gerald C. O'Neil, 640 City National Bank Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Arthur H. London, 1105 W. Main St., Durham.
Secretary: Dr. Jay M. Arena, 604 W. Chapel Hill St., Durham.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Boggs, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hilla Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. L. E. Sutton Jr., Medical College Hospital, Richmond.
Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Andrew Amick, 1021 Quarrier St., Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg., Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND PEDIATRIC SECTION

Chairman: Dr. J. W. Epstein, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Virginia Barker, City Hospital, Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Jacob H. Turner, 121 W. 197th St., New York.
Secretary: Dr. Harry S. Pizer, 1726 Davidson Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Second Wednesday of each month except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Kenneth G. Jennings, 159 Midwood St., Brooklyn.
Secretary: Dr. Joseph Battaglia, 713 Bushwick Ave., Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday each month except May, June, July, August and September.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St., Syracuse.
Secretary Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Morley D. McNeal, 2 N. Sheridan Rd., Highland Park, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Cincinnati Pediatric Society

President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.
Secretary: Dr. T. Selkirk, 3530 Reading Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati.
Time: On call.

Dallas Pediatric Society

President: Dr. Robert A. Knox, 3701 Fairmount Ave., Dallas 4, Texas.
Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Belfort Pl., Dallas 4, Texas.
Place: Children's Medical Center. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. John J. Pollack, 650 Maccabees Bldg., Detroit, Mich.
Secretary: Dr. Philip J. Howard, 2799 W. Grand Blvd., Detroit, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatrics Section (Atlanta, Ga.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St. N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: College Inn, Houston. Time: Fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Edwin H. Schorer, 1103 Grand Ave., Kansas City.
Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St. Joseph, Mo.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Milo B. Brooks, 1033 Gayley Ave., West Los Angeles.
Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles 26.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Abraham M. Litvak, 1145 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month, October to April, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry A. Spigel, 2647 Connecticut Ave., Washington, D. C.
Secretary-Treasurer: Dr. Perry W. Gard, 2520 Woodley Rd., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. M. G. Peterman, 411 E. Mason St., Milwaukee 2.
Secretary-Treasurer: Dr. B. J. Malnekoff, 3213 N. Marietta Ave., Milwaukee.
Place: Milwaukee Athletic Club. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Howard Craig, 175 E. 79th St., New York.
Secretary: Dr. Alfred E. Fischer, 73 E. 90th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. John Mott Rector, 2000 Van Ness Ave., San Francisco.
Secretary: Dr. George Bates, 490 Post St., San Francisco 2.
Time: Four times yearly.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Carl Fischer, Greene and Coulter Sts., Germantown, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday in January, March, May and November.

Pittsburgh Pediatric Society

President: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. William L. Bradford, 260 Crittenden Blvd., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Donald D. Posson, 222 Chili Ave., Rochester 11, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Peter G. Danis, 634 N. Grand Ave., St. Louis 3.
Secretary-Treasurer: Dr. H. Ewing Wachter, 3720 Washington Ave., St. Louis.
Place: St. Louis Medical Society Bldg. Time: Third Thursday of each month from November to June.

Seattle Pediatric Society

President: Dr. Frederick B. Joy, Stimson Bldg., Seatt
Secretary: Dr. Sherod M. Billington, Medical Den Bldg., Seattle.
Place: College Club. Time: Third Friday of ea month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Jeanette Harrison, 1136 W. 6th S Los Angeles.
Secretary: Dr. Henry F. Gallagher, 1930 Wilsh Blvd., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: Fi Wednesday in January, March, May, September a November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Campbell Harvey, 35 W. Huron S Pontiac, Mich.
Secretary: Dr. Harry A. Towsley, University of Mic igan, Department of Pediatrics and Communicab Diseases, Ann Arbor, Mich.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonke N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highla Rd., Rye, N. Y.
Place: Grasslands Hospital, Valhalla, N. Y. Tim Third Thursday in October, December, February a April.

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CONTENTS

PAGE

PROGERIA: CLINICAL, METABOLIC AND PATHOLOGIC STUDIES ON A PATIENT. NATHAN B. TALBOT, M.D.; ALLAN M. BUTLER, M.D.; EDWARD L. PRATT, M.D.; E. A. MACLACHLAN, M.D., AND J. TANNHEIMER, M.D., BOSTON 267

PYODERMIC MYIASIS IN CHILDREN: OBSERVATIONS WITH SPECIAL REFERENCE TO TÓRSALO. LEON GOLDMAN, M.D., CINCINNATI 280

SULFATHIAZOLE OINTMENT FOR PREVENTION AND TREATMENT OF PYODERMAS OF NEWBORN INFANTS: RESULTS OBTAINED WITH FIVE PER CENT SULFATHIAZOLE IN AN OIL IN WATER TYPE EMULSION BASE. CHARLES A. WEYMULLER, M.D., AND ELIZABETH J. ITTNER, M.D., BROOKLYN 283

CASE REPORTS:

OBSTRUCTIVE PULMONARY EMPHYSEMA ASSOCIATED WITH PNEUMONIA IN CHILDHOOD. JEROME S. LEOPOLD, M.D., AND EMIL A. KRATZMAN, M.D., NEW YORK 287

CHRONIC PYELONEPHRITIS WITH RENAL ACIDOSIS. M. G. PETERMAN, M.D., MILWAUKEE 291

PROGRESS IN PEDIATRICS:

AMYOTONIA CONGENITA (OPPENHEIM): REPORT OF FIVE CASES WITH NECROPSY; DISCUSSION OF THE RELATIONSHIP BETWEEN AMYOTONIA CONGENITA, WERDNIG-HOFFMANN DISEASE, NEONATAL POLIOMYELITIS AND MUSCULAR DYSTROPHY. WILLIAM F. BURDICK, M.D.; DOROTHY V. WHIPPLE, M.D., AND WALTER FREEMAN, M.D., WASHINGTON, D. C. 295

ABSTRACTS FROM CURRENT LITERATURE 308

SOCIETY TRANSACTIONS:

SOCIETY FOR PEDIATRIC RESEARCH 322

OBITUARIES:

LOUIS FISCHER, M.D. 331

BOOK REVIEWS 332

NEWS AND COMMENT 333

DIRECTORY OF PEDIATRIC SOCIETIES 334